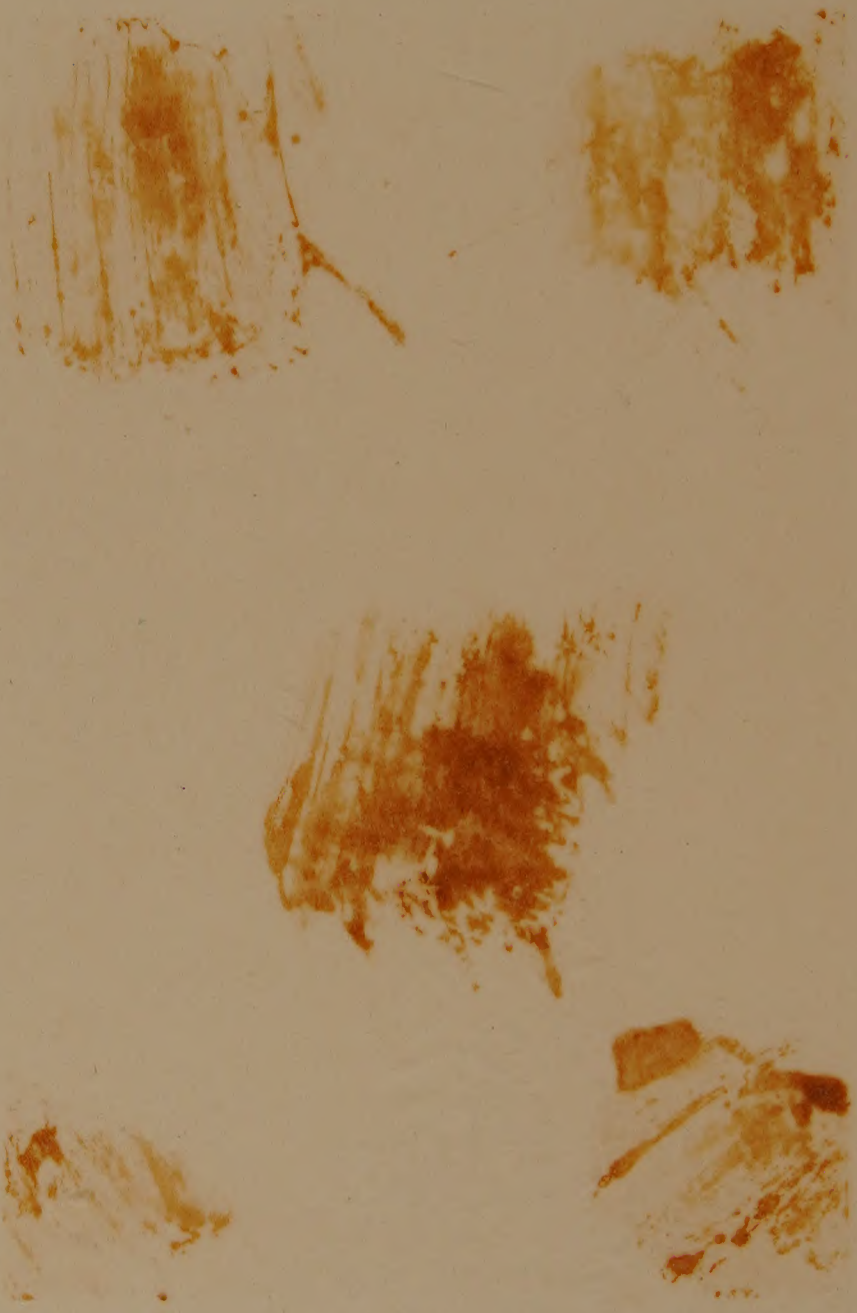

RADIUM
IN GENERAL PRACTICE

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BY

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WITH TWENTY-EIGHT
ILLUSTRATIONS

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MY WIFE

PREFACE

THE author has prepared this treatise on the elements of radium therapy, having in view the following objects:

First, to make available to the general practitioner the elements of radium therapy in the daily practice of medicine in such a form that he may quickly refer to the therapeutic possibilities in the use of radium in any particular disease and weigh its value in comparison with other available methods.

Second, these elements are stated only in brief. Exhaustive technical discussion is avoided.

Third, radium therapy is making progress. The indications and technic are approaching standardization in the conditions more commonly recognized as suitable for this form of treatment.

Fourth, the effort is made to furnish readable, understandable data on radium indications, technic, reaction and prognosis in the lesions more commonly treated with this agent.

Fifth, the author has attempted in this little work to gather together information from numerous reports and from personal observation and experience, in order that the maximum benefit may be derived from the use of radium, a very valuable therapeutic agent.

Sixth, the radical change in the field of physics brought about by recent and current investigations in radioactivity is exerting an important influence in the field of biology and in the practice of medicine. Should there occur changes in the theories relating to biology and medicine to any extent commensurate with those recently injected into the field of physics by studies in radioactivity, the medical profession as a whole may find itself unprepared for these new concepts in their relation to the fundamental phenomena within the human body in all its pathologic changes.

Seventh, in view of these possibilities the author hopes that this publication may prove to be a forward step toward a true evaluation of radium in the treatment of disease; that it may result in the assembling of reliable data and experiences; that it may stimulate further research into the possibilities of radium therapy; that it may aid in combating propaganda against so valuable an agent and that it may help to anticipate the changed fundamental concepts in the practice of medicine which may follow the changed concepts in the field of physics due to studies in radioactivity.

A. James Larkin

Chicago, Illinois
September, 1929.

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PART I

GENERAL CONSIDERATIONS

GENERAL CONSIDERATIONS

Mechanics of Radium

Radium is an element with an atomic weight of 226, spontaneously disintegrating, emitting alpha particles which are helium atoms minus two electrons, and beta rays which are negative electrons; in certain stages of the disintegrative process gamma waves of ether are emitted. The alpha rays are of little value in medical treatment except in internal administration where their action and value as well as any untoward effects are yet to be reliably ascertained. They are completely absorbed by the walls of all applicators in daily use in the practice of radium therapy; 0.03 mm. of aluminum absorbs all alpha particles.

Beta rays are negative electrons traveling at seven-tenths to nine-tenths of the velocity of light. Fifty per cent of the beta rays are absorbed by 0.1 mm. of lead or 1.0 mm. of soft tissue. Each additional 0.1 mm. of lead or 1.0 mm. of soft tissue absorbs 50 per cent of the remaining beta rays. Thus, less than 0.1 per cent of these rays penetrate 1.0 mm. of lead or 1.0 cm. of soft tissue.

All substances absorb beta rays according to their densities. Therefore, to absorb 50 per cent of the beta rays from radium, the following thicknesses of the common metals used for screening may be employed:

Steel	0.2 mm.
Brass	0.2 mm.
Silver	0.1 mm.
Monel metal	0.45 mm.
Lead	0.1 mm.
Gold	0.06 mm.
Platinum	0.05 mm.

To absorb 99.9 per cent of all beta rays, ten times the thicknesses of the above-mentioned metals is required, namely:

Steel	2.0 mm.
Brass	2.0 mm.
Silver	1.0 mm.
Lead	1.0 mm.
Gold	0.6 mm.
Platinum	0.5 mm.

There is frequent use for the hard beta rays, though only 10 to 15 per cent of the hard beta rays are desirable. Screens transmitting these hard beta rays and absorbing the softer rays are as follows:

Steel	0.6 mm.
Brass	0.6 mm.
Silver	0.3 mm.
Monel metal	0.45 mm.
Lead	0.3 mm.
Gold	0.18 mm.
Platinum	0.15 mm.

With few exceptions the screening may be classified as follows in radium therapy: first, no screen, as when bare plaques are employed; second, screens transmitting 10 to 15 per cent of the hard beta rays as already mentioned; or third, screens absorbing all beta rays.

In this text the screen absorbing all beta rays is called "the beta ray screen."

In skin lesions where short applications are made and mild or alterative effects only are desired, screens absorbing 10, 20 or 30 per cent of the beta rays may be employed by those expert and experienced in a large amount of radium work in dermatology. For ordinary purposes the absorption of less than 50 per cent of the beta rays is unnecessary. The dosage can usually be regulated by the time of the exposure rather than by varying the screen. Simplicity in screening with many variations in the length of the exposure or the distance between the radium and the lesion to obtain various effects serves better in ordinary practice than a multiplicity of screens.

Gamma rays are ether waves having the velocity of light. The wave length is estimated at from 0.01 to 0.001 Ängstrom units (an Ängstrom unit equals 1/10,000,000th of a millimeter), thus having a penetration from 5 to 50 times that of the hard roentgen rays now used in therapy. Thirteen millimeters of lead absorb 50 per cent of the gamma rays. Thirteen centimeters or ten times 13 millimeters absorb 99.9 per cent of the gamma rays.

In therapy it is rarely necessary to absorb the gamma rays. Therefore the beta ray screen as employed in the various diseases discussed in this text refers to a screen

absorbing all beta rays; i. e., a screen of 2.0 mm. of brass, 1.0 mm. of silver, or 0.5 mm. of platinum or their equivalent in other metals. Probably the most common beta ray screen equivalent is the screen of 1.0 mm. of brass in which is placed radium element in needles of steel, platinum or gold or the common 0.5 mm. silver capsule furnished by radium producers with glass tubes containing radium element. The resultant screen then has an effect equal to 1.0 mm. of silver or lead, namely, the beta ray screen.

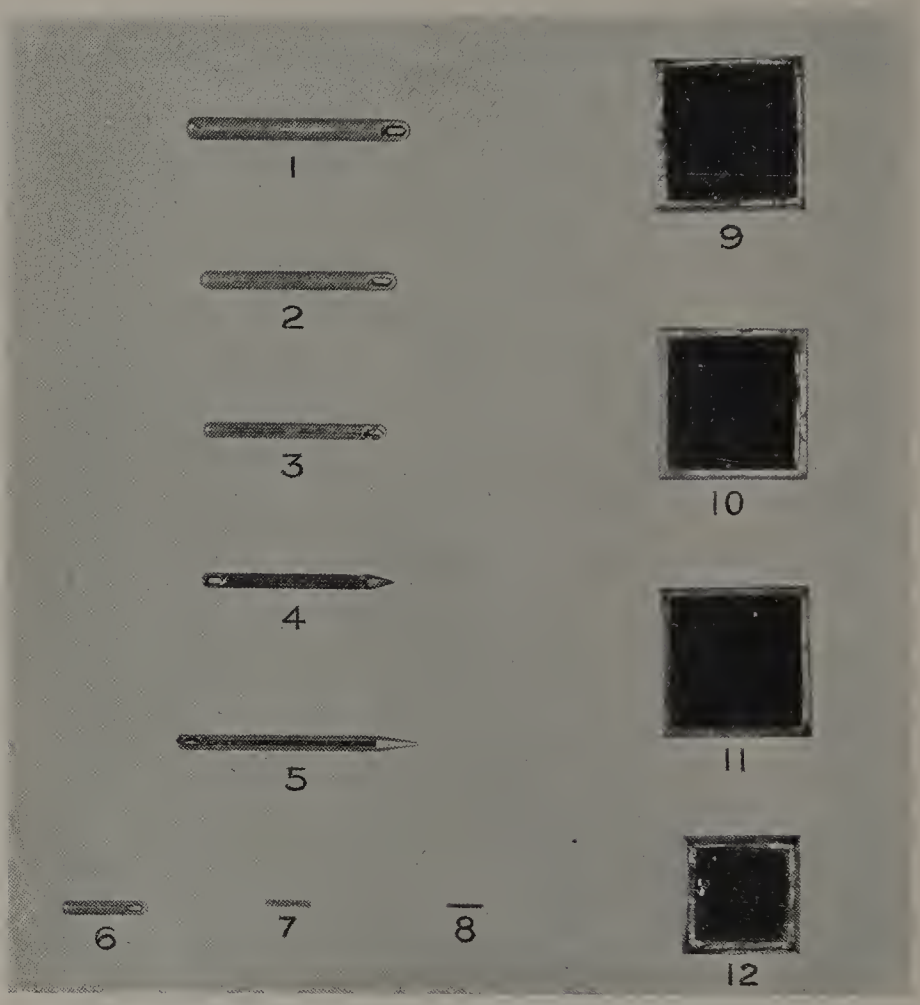
Superscreens of 1, 2 or even 3 mm. of platinum or equivalent in other metals are used when intensive deep external irradiation is given. From 5 to 15 per cent of soft gamma rays are thus absorbed by the screen. Dosages much greater in milligram-hour reckoning can be given without visible skin reaction.

Biologic Reactions

The biologic reactions due to radium may be classed under four headings, under which an attempt will be made to explain all therapeutic results now obtained.

1. *Necrosis.* Living cells exposed to radium rays in sufficient amounts disintegrate and die. It is believed that the ionic imbalance and consequent disintegration set up within the tissues bring about this reaction. Pathologic cells require for their destruction less radiation than normal cells of the same type. Susceptibility to radium rays varies greatly from the sensitive lymphatic and sex cells to the very resistant bone and nerve tissues. Though all pathologic cells seem to be more susceptible than the normal there is a wide variation in reaction between the sensitive lymphosarcoma and those of mixed-cell tumors on the one hand and the resistant bone sarcoma and neurogenic sarcoma on the other.

Attempts have been made to classify tumors in relation to their radiosensitiveness in terms of percentages of erythema dose required to destroy them, but with questionable success. However, some general rule must govern the therapeutist in his initial applications to various lesions. All degrees of reactions within the cells from necrosis to no reaction at all are obtained with decreasing amounts of radiation.



FIGS. 1–12. Radium and radon containers most commonly used.

FIG. 1. 50 mg. platinum tube, actual size, 0.5 mm. wall thickness (beta ray screen).

FIG. 2. 25 mg. platinum tube, actual size, 0.5 mm. wall thickness (beta ray screen).

FIG. 3. 12.5 mg. platinum tube, actual size, 0.5 mm. wall thickness (beta ray screen).

FIG. 4. 12.5 mg. monel needle, actual size, 0.4 mm. wall thickness (87.5 per cent beta ray screen).

FIG. 5. 2 mg. platinum needles, 31.5 mm. long by 1.6 mm. in diameter, 0.5 mm. wall thickness (beta ray screen). This type of needle is used when multiple sources of irradiation are desired.

FIG. 6. 1.3 mg. platinum removable radium implants, actual size, 0.5 mm. wall thickness (beta ray screen).

FIG. 7. Gold radon implant, 0.3 mm. wall thickness (97 per cent beta ray screen) for permanent embedding in tissue.

In short, all may be considered as degrees of inhibition, since there is little evidence that small doses stimulate any cell.

Results in treatment of carcinoma sometimes suggest stimulation by the rays, but, as yet, no clinical or experimental evidence substantiates the theory, at least none with reference to individual cell stimulation. The course of necrosis consists of swelling with accompanying inflammation or local erythema followed by nuclear and cytologic disintegration, vacuolization, liquefaction, cell rupture, and absorption followed by replacement with fine fibrous tissue. A caustic action is obtained by implants of radon in which complete necrosis and subsequent fibrosis occur in the immediate vicinity of the tiny glass seeds, for a surrounding distance varying with the amount of radon in the implant and the susceptibility of the tissue. Cautery action is obtained from needles and even from heavily screened tubes when the dosage is sufficient. Necrosis of susceptible tissue may be obtained by heavy screening, even through normal skin, especially when cross-fire technic is used viz., irradiating from several different angles through normal tissues. However, necrosis in this instance is to be distinguished from a cautery effect where all normal as well as pathologic cells are destroyed. This latter is important therapeutically when one considers that the complete cautery action devitalizes normal structures which may, and probably do, play an important part in building up resistance against recurrences. For this reason in the advancement of our technical knowledge, cautery destruction seems to be losing ground in the therapy of malignant processes. Necrosis of malignant cells only or inhibition sufficient to enable the bodily resistance to overcome the invasion seems to be the goal now sought. The rapidity and completeness of cellular destruction

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FIG. 8. Glass radon implant (no beta ray screen) for permanent embedding in tissue.

FIG. 9. 10.0 mg. full strength plaque, actual size.

FIG. 10. 5.0 mg. half strength plaque, actual size.

FIG. 11. 2.5 mg. quarter strength plaque, actual size.

FIG. 12. 5.0 mg. full strength plaque, actual size.

may well be observed in the stained blood specimens from splenomyelogenous leucemia during the first few days following adequate radium treatment.

2. *Endarteritis.* Radium irradiation causes the intima of blood vessels to undergo hypertrophy and proliferation to such an extent that the tiny vessels become occluded and the result is a permanent obliteration of the lumen. Pathologic vessels found in hemangiomatous tissues are most susceptible, but normal vessels also yield; and this phenomenon may be responsible for the therapeutic results obtained in fibroids, and to a much lesser degree perhaps in exophthalmic goiter. Even in carcinoma the rôle of this property of radium rays may be greater than we suspect.

3. *Analgesic Effect.* Almost daily every radium therapist observes relief from pain but often loses sight of it until some striking and unquestioned example presents itself. The pain of neuritis and neuralgia often yields to small doses of radiation. Herpes zoster and pruritus in their reactions to the rays often indicate that the nerve endings or even the nerve trunks experience an elevation of their threshold of sensitiveness or inhibition of their activity when radiation is applied in relatively small doses. The author recalls a case of metastases to the spine in which, following radium applications, relief from pain was repeatedly observed in such a short time, namely thirty-six hours, that it was impossible to attribute the effect to marked cell change occurring within the malignant tissue.

Relief from pain in arthritis often quickly follows the injection of sufficient amounts of radium into the blood stream and even the placing of a certain amount of radium externally over the affected joints may relieve the pain. More use should be made of this analgesic property of radium.

4. *Alterative.* For lack of a better term "alterative" is used to designate that property which is responsible for good results in such conditions as eczema, tuberculous ulcers, tuberculous glands, and many other conditions which require only a small amount of irradiation. Local leucocytosis may play a part, or it may be the increased sensitiveness of the cells in their pathologic state, or there

may be such a thing as secondary general stimulation of cells to more vigorous performance of their function of resistance against invasion. Inhibition of nerve function may explain the result; but at any rate the term alterative may be employed to designate this property of radium radiation which is extremely useful in various lesions.

Methods of Application in General

1. *External Application (Deep Therapy).* Beta ray screen at a distance from the skin. One thousand milligram-hours at 1 inch distance over each area containing 2 square inches may serve as a standard, increasing or decreasing the distance directly as the milligram-hours.

From 1.0 to 4.0 gm. of radium in one block or "pack," screened with 2 mm. of brass, irradiating at 6, 10 or 15 cm. distance, results in a smaller difference between the skin dose and that delivered to deep-lying lesions. Dosages, using this technic, may approach 8000 mg.-hr. over each 70 sq. cm. at 6 cm. distance; 16,000 mg.-hr. at 10 cm. distance; and 24,000 mg.-hr. at 15 cm. If 2 mm. of lead screen are used, the dosage may be 25,000 at 10 cm. and 50,000 at 15 cm. distance (Quick, Failla). Such deep irradiation gives greater promise of success in deep-lying lesions. The late effects of such irradiation upon normal structures and the general body mechanism are as yet unknown. It is not likely that there are any detrimental late effects.

2. *Surface or Contact Application.* Tube or plaque containing element or radon laid immediately in contact with the lesion employing no screen at all or a screen sufficient to absorb all beta rays.

3. *Cavity Application.* Tube of element or radon variously screened for application within the body cavities, viz., uterus, rectum, esophagus, etc.

4. *Interstitial Application.* Needles containing element or radon, or tiny glass, platinum, or gold implants placed within the lesion through the skin or mucous membrane, or through an incision and removed in the case of the needles or left permanently in place in the case of the implants. Gold implants with a wall 0.3 mm. in thickness, transmitting

3 per cent of the beta rays, may be used in the same manner as the glass implants with less caustic necrosis because soft beta rays are absorbed by the gold wall. They are far superior to glass implants on this account. Platinum needles of 0.5 mm. wall thickness, containing 1 mg. of radium per linear centimeter may be inserted 1 cm. apart and left in place five to seven days, thus delivering gamma rays only in dosage of from 120 to 170 mg.-hr. per cubic centimeter of tissue. They are less caustic than implants and no foreign body remains.

5. *Internal Administration.* Intravenous or oral administration of radium element in solution or of radon in drinking water.

6. *Inhalations or intravenous or oral administration of radon* or its absorption from radioactive bath water.

The remote effect of the retention in the body of appreciable amounts of radium element or the active deposit of slow decay are not surely known. It may be possible for deleterious results, as yet unknown, to follow in later years as the result of the ingestion of radium or radon.

In determining the indications for radium treatment, the method of application and the dosage, the radiologist must be guided by a knowledge of the biological reactions produced in human tissues by radium and of the gross and minute anatomy of the lesion, as well as by a familiarity with the technic of administration of radium. He must make or be supplied with sound clinical observations as to the patient's general and local physical condition. He must know what can be accomplished by other methods in dealing with the pathology in hand in order to make a conservative estimate as to whether radium therapy will better serve the indications.

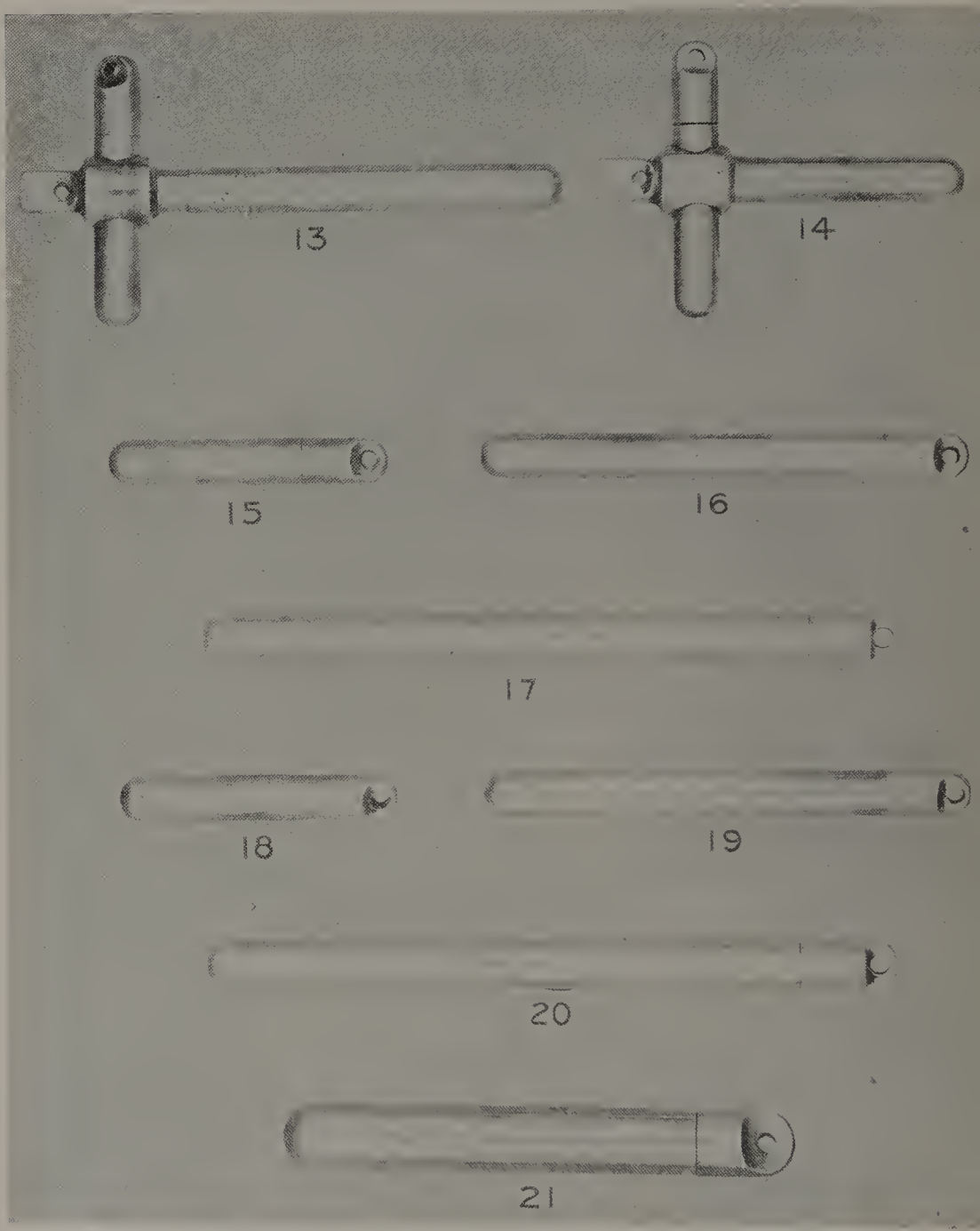
General Technic

A few general rules as to technic may be mentioned. During treatment all radium applicators should be secured by mechanical means to external parts of the body so that by no possible chance may the radium applicator become displaced or lost. Loss of radium is prevented only by systematic, painstaking care. Responsibility for the radium

should be placed on as few individuals as possible. It should be kept in a secure place under lock, preferably in a lead-protected safe. Six inches of lead gives 100 per cent protection. Frequent checking of the radium is necessary; and the radium should be so stored that it can all be seen at a glance, thus reducing the time of exposure of the checker. The radium should be removed from the patient by the one who inserted it, or by one who was present at the insertion. It should be checked immediately with the written record on the patient's chart or some suitable written description of the number and identification of the radium as it was applied. After checking for full identification it should be placed at once in the permanent receptacle maintained for the purpose. Radium insurance policies demand supervision during the application. Most losses are due to carelessness, thoughtlessness or momentary lapse on the part of those accustomed to handle the radium. If the one who removes the radium will at once place it in its permanent receptacle, leaving the dressing of the wound to an assistant or nurse, the precaution will prevent many radium containers from going into the furnace with the dressings. Prevent the capsule from being swallowed or retracted into a sinus, the bladder, the uterus, the peritoneal cavity, or the large bowel by a long cord, wire, or other mechanical means. The loss of radium within the patient's body practically always requires immediate mechanical removal. Its loss in the normal gastrointestinal tract may constitute an exception to this rule, when the amount of radium is under 50 mg. and the screening is of the beta ray type.

For the individual problems relating to various lesions amenable to radium treatment, the reader is referred to the text under the diagnosis and anatomical location of the lesion in question. All discussions of the radium treatment of individual lesions follow the accompanying outline:

1. *Pathology* (brief).
2. *Indications for Radium Therapy:*
   (a) Applications of the properties of radium to the pathology.
   (b) Contraindications.



FIGS. 13–21. Typical applicators composed of aluminum screens suitable for various combinations of radium containers.

3. *Application:*
   (a) General technic.
   (b) Methods employed.
   (c) Dosage.
   (d) Number of applications.
4. *Reaction:*
   (a) General—extent and course.
   (b) Local—onset, degree, duration, course, complications, termination, recurrences.
5. *Prognosis:*
   (a) Immediate.
   (b) Remote.

The *diagnosis* of the various lesions is not discussed in this treatise but it must be established as nearly as possible beyond peradventure of doubt before radium treatment is instituted.

1. In the modern practice of medicine biopsy is the only incontrovertible evidence of diagnosis.

2. When biopsy is impossible on account of the inaccessibility of the disease or on account of danger of dissemination, competent consultation may be recognized as satisfactory.

Fig. 13. Cervical cross arm aluminum screen (secondary ray screen,) actual size, with long uterine arm, to hold platinum radium tubes, 50 mg. in cross arm and 100 mg. in upright.

Fig. 14. Cervical cross arm aluminum screen (secondary ray screen), actual size, with short uterine arm, to hold platinum radium tubes, 50 mg. in cross arm and 50 mg. in upright.

Fig. 15. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold one 50 mg. platinum radium tube.

Fig. 16. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold two 50 mg. platinum radium tubes in tandem.

Fig. 17. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold three 50 mg. platinum radium tubes in tandem.

Fig. 18. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold one 25 mg. platinum radium tube.

Fig. 19. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold two 25 mg. platinum radium tubes in tandem.

Fig. 20. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold three 25 mg. platinum radium tubes in tandem.

Fig. 21. Aluminum screen (secondary ray screen), actual size, for cavity or surface application, to hold four 50 mg. platinum radium tubes in tandem-team.

In this event all laboratory aids ruling out other possibilities should be used.

3. Familiarity by training and experience on the part of the physician specializing in the field in which the lesion lies will often justify the diagnosis. This is more applicable to the non-malignant lesions in which radium may be used. No undiagnosed lesion should be treated with radium.

General Management of a Radium Case. The general management of a radium case may be a simple or a tremendous task, depending upon the severity of the lesion and upon the prognosis. Many superficial and non-malignant lesions require little more than an explanation of the clinical course of the reaction and a description of the end results sought. Frequent observations of the progress of the treatment may be unnecessary.

Cases of more serious import require careful description of the probable progress of the reaction, together with weekly or bi-weekly observations and consultations with the patient. Medication, advice, and encouragement, frequently given, aid materially in the progress of the patient through a troublesome period. Cases of serious import, grave prognosis, and impaired general health require daily observation in the hospital or under competent nursing care.

In addition to efficient general medical and expert local attention, the patient calls upon the radiologist for encouragement and judicious explanation of the various symptoms, which the patient attributes in most instances to the treatment rather than to the disease. A careful psychologic analysis of the patient's mental processes must be made if cases of grave prognosis are to be successfully managed. Consultations with internists, surgeons and neurologists should be welcomed and sought during the progress of a serious case. Close cooperation between the radiologist and the surgeon, the internist, the gynecologist, or the specialist in whatever field the lesion lies, will bring about a better selection of cases for treatment, better understanding of the limits and possibilities of radium therapy and its more efficient use.

Contraindications to Radium Treatment

Contraindications to irradiation with radium may be classified as general and local.

Among the general contraindications *cachexia* is of the greatest importance. No cachectic patient should be irradiated with radium except in very rare instances, and these only after the most deliberate consideration.

Usually a *weakened and "rundown" condition* contraindicates radium treatment. If the patient's condition is due to the lesion for which this radium treatment is to be given, the possible benefit to be derived must be weighed carefully against the possible harm coming from the general effect of the treatment. As a general thing, weakened patients do not rally well from irradiation. Local lesions do not do well after irradiation if the patient does not endure the general and local effects of irradiation well. Ulcerations do not heal. Elimination of the products of the local catabolic process is imperfectly accomplished. General intoxication may render the patient more miserable and actually hasten the end, unless his condition is such that he can endure severe reactions well.

Anemia is a contraindication to extensive irradiation This is especially true in the case of malignant lesions. Careful determination of the extent and cause of the anemia must precede the irradiation. Milder degrees of anemia require careful consideration of the patient's toleration of the treatment as against the benefits to be derived therefrom.

White blood cell counts below 5000 contraindicate radium treatment. *Leucopenia* below 3500 is a condition fraught with great danger to life.

In diseases such as diabetes, severe nephritis, general paresis, extreme obesity, advanced myocarditis, active pulmonary tuberculosis, marked arteriosclerosis or any *generally debilitating disease*, all radium treatments except those of very minor nature are hazardous and to be most carefully considered before administration.

General sepsis contraindicates radium treatment.

Local inflammation or infection contraindicates local irradiation until adequate treatment eradicates it. Acute, subacute or chronic inflammation in adjacent structures

contraindicates radium treatment. This is especially true if free drainage is not obtainable. Salpingitis contraindicates intrauterine radium treatment.

Fig. 22. Lead window screen for use with plaques.

Unknown amounts of radium or roentgen-ray treatments previously given prohibit irradiation with radium until after the lapse of sufficient time, generally three or four weeks if there is no visible evidence of reaction to the previous irradiation. There is no exception. Details of technic and the time of the previous irradiation must be known.

In general radium treatments should not be given unless there is abundant evidence that treatment gives promise of a hope of cure or of unquestioned improvement in the condition of the patient. Palliative treatment is often justifiable. If there is doubt, the aid of competent consultants of large experience in radiology is imperative.

Dangers of Radium Applications

1. *Loss of Radium within the Body of the Patient.* This is one of the dangers which is ever present and which must always be guarded against. The radium applicator must be firmly attached to some object or part of the patient's body during the application so that it is impossible to lose control of it at any time from the very beginning of the insertion until the radium is finally removed. The string or wire attached to the radium should be fastened to the patient's body by means of adhesive tape, bandage, or other mechanical means. If there are several applicators used simultaneously, the wires or cords may be tied together and all anchored to the patient. Especial care is necessary when applications are made to the nose, mouth or throat to prevent sudden swallowing or inhaling of the radium or radon. Uterine, rectal, bladder and esophageal applicators should have strong cords or wires of generous length so that there will be no fear of breaking

during the removal of the radium even though resistance should be encountered in its withdrawal. All joints, knots or hinges which are part of the radium applicators should be of such nature that unscrewing, unhinging, unlocking or loosening in any manner cannot possibly occur. The inadvertent loss of radium within the patient's body is almost *per se* evidence of lack of due care and diligence in the treatment of the case.

In inserting radon implants, the tiny applicator should be pushed well up into the barrel of the inserter and the shaft held in an upright or horizontal position until the puncture has been made. Ordinarily the implant will remain in the inserter even if it is inverted; however, a sudden jar might result in dropping the implant in an undesirable place or in losing it unnoticed and thus a false insertion might be made. The eye of the operator should be focused on the point of the inserter until the puncture has been made in order that he personally may know that the implant has actually been delivered within the tissues.

If a radium applicator should be out of control in the uterus, abdominal cavity, or buried in any solid organ, it must be removed by incision or other mechanical means. If the radium applicator is out of control in the gastrointestinal tract, including the normal rectum, it may be allowed to continue along the course of the bowel aided by catharsis and checked frequently by fluoroscopic or roentgenographic examination. If the radium becomes lodged for any length of time over an hour or so, measures must be taken to remove it mechanically. Radium out of control in a carcinomatous rectum will probably not be expelled and must be recovered mechanically.

2. *Excessive dosage,* resulting in perforation of a viscus, or a blood vessel of considerable size, or in extensive destruction of a vital organ. Destruction of the thin vesicovaginal or rectovaginal wall should be avoided since fistulae which may be attributed to the radium are highly undesirable. Perforation of the thin wall of the esophagus, bowel or urinary bladder may result in fatal infection in the surrounding tissues. Dosages above 500 mg.-hr., even with the beta ray screen, administered to thin-walled organs are to be avoided.

Applicators employed in these sites should have thick walls of aluminum or other material so that the distance dispersion is great enough to prevent a perforation through a cautery effect. A total of 1000 mg.-hr. at 1 inch distance with the beta ray screen is ordinarily a safe dosage. If the distance is reduced the dosage is lessened by its square, e. g., at ½ inch distance the dose should be 250 mg.-hr. If the wall of the viscus is completely involved in the malignant tissue and sufficient dosage is given to destroy the malignant tissue, then, of course, perforation is inevitable and should be reckoned with at the outset. Such applications should be made advisedly and with full consciousness of the probable outcome. Severe, deep, and widespread necrosis of any surface is to be avoided, whether it be skin, mucous membrane or other structure. Ulcerations 1.0 or 2.0 cm. in diameter, even though deep, usually heal. Larger areas heal with difficulty over several weeks' or months' time, but they eventually are cured if not complicated by malignant disease. Late slough, appearing six to eighteen months after heavy irradiation or too frequently repeated treatment, occasionally occurs as a distressing complication, but fortunately it is uncommon.

Excessive and painful reactions following extensive irradiation are often more distressing to the patient than the disease itself. Whether the disease is curable or incurable, irradiation which results in obstinate deep ulcerations rendering life miserable on account of pain and discharge is not justifiable. If a lethal dose cannot be delivered to malignant tissue without widespread destruction of adjacent normal structures, it were better not given. Excessive dosage does not improve immediate or end results.

3. *Pyogenic infection*, especially if it is acute, or if the infected area is not freely open to drainage, will undergo an acute exacerbation as the result of irradiation. Salpingitis will flare up, often resulting in abscess formation, if a radium treatment is given within the uterus. If there is an infectious process present in the tissues to be irradiated, or in adjacent structures, it should be cleared up before radiation treatment is instituted. Streptococcus infection may be lighted up and disseminated by irradiation, especially if of the interstitial type.

4. *Fever* above 101.5°F. renders irradiation dangerous.

5. *Leucocyte counts below* 3500 contraindicate radium treatment. Sudden death may ensue.

6. *Proximity to delicate structures.* Radium applicators must not be inserted within 1.0 cm. distance of blood vessels of size unless they are heavily screened and placed there advisedly. Caustic necrosis of the eyeball, of cartilage and of nerve trunks must be avoided unless it is the deliberate intention to sacrifice them in the interest of a permanent cure.

7. *Danger to the operator* from exposure to radium is fairly well known. Radium applicators should never be touched with the fingers, should never be carried in the hand except for the very briefest time and then protected by metal or carried at a considerable distance, 1 to 2 feet, from the body. The user of radium should keep it as far away from his person as is possible and for as much of the time as is possible. Continued short exposure to radium results in dry skin, brittle and fissured nails, and in extreme cases in ulceration with pain and with the remote possibility of malignant degeneration of the member. Exposure to large amounts of radium over a long period of time (several hundred milligrams for years) may result in weakness, malaise, irritability, backache, low leucocyte count and in extreme cases to fatal primary anemia. Radium rays diminish in intensity as the square of the distance; consequently, distance is the most efficient protection for the user of radium. Radium should be handled with forceps and it should be kept as far from the user as possible when not in use.

8. Large tumors exerting *pressure on vital structures* should be irradiated only after the most careful deliberation and then only in desperate cases. Fibroid tumors of large size swell when treated with radium and in general should not be irradiated. The temporary engorgement of mediastinal tumors after irradiation may cause dyspnea, venous stasis, or cardiac embarrassment. Here, again, the risk of serious outcome following the temporary swelling of the tumor must be carefully weighed against the ultimate benefit to be obtained from the treatment.

PART II

GENERAL DISEASES

GENERAL DISEASES

Banti's Disease

The *diagnosis* is not discussed in this outline but it should be established by every possible means (see p. 13).

Pathology. Banti's disease is a condition characterized by marked enlargement of the spleen, anemia, and in some cases cirrhosis of the liver, portal in type. The disease develops slowly over a period of from three to ten or twelve years. The splenic enlargement may be enormus. There is marked hyperplasia of the pulp and greatly increased fibrosis; other changes, such as venous sinus enlargement or compression, calcification and cyst formation are often found. The cirrhotic enlargement of the liver develops late in the disease after the anemia has become marked. Terminally the liver may decrease in size. Ascites is a late or terminal finding. The white cell count of the blood is but little changed and the lymphatic glands are usually unaffected.

Radium Indications. The gamma rays of radium possess the penetration and the properties capable of causing inhibition, atrophy and disintegration of the hyperplasia of the spleen. Reduction in size of the spleen with marked improvement has frequently been accomplished by gamma ray irradiation of the spleen in Banti's disease.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used (see p. 15).

Application. Deep external irradiation with gamma ray comprises the only practical method of non-surgical treatment. From 1000 to 1200 mg.-hr. at a distance of 1 inch, over each area of 2 sq. in. with the beta ray screen may serve as a standard dosage. The total irradiation may vary in amount from 6 to 10 or even 20 gm.-hrs., according to the size of the spleen. Renewed treatment is indicated at intervals of one to six months, depending upon the size of the spleen, the skin reactions, and the general condition of the patient. Where splenectomy is contemplated, useful reduction in its size may be accomplished by irradiation as a

preoperative measure. Repeated doses may be equal in amount or reduced, according to the previous reactions and results.

Reaction. With dosage amounting to many gram-hours the general reaction may be marked with malaise, anorexia, nausea, vomiting and long-continued weakness and constipation from which recovery may be protracted. Anemia may be temporarily increased and accompanied by a transient leucopenia. Locally, some splenic enlargement may be evident during the second week, due to temporary inflammatory swelling attending the reaction to the gamma rays. By the third and fourth weeks reduction in size of the spleen is often apparent. Retraction of the splenic margin, as well as decrease in the anteroposterior diameter, occurs but usually not to the satisfactory extent accomplished in myologenous leucemic splenomegaly. At operation or autopsy, adhesions between the spleen and the parietal peritoneum are not uncommon. Anemia may be temporarily increased, but the blood picture usually improves with splenic shrinkage and the general improvement which ordinarily follows adequate irradiation of the spleen. Temporary leucopenia during the first week or ten days is not uncommon. A rise of temperature may result from irradiation but is not of grave import. The decrease in the size of the spleen is maintained for from one to six months, when re-enlargement occurs. A second irradiation yields decreased results with temporary decrease in size of the spleen and with some general improvement, only to recur in a few months and so on until eventually the outcome is fatal. Irradiation over the liver yields no good results. Unfavorable cases do not respond with reduction in size of the spleen or with any general improvement.

Prognosis. Banti's disease is relatively rare and reports of radium treatment few, but improvement has been favorable in the majority of the cases reported. A few do not seem to be at all affected, these usually being of long standing with markedly hard fibrous changes in the spleen accompanied by enlargement of the liver of relatively long standing. Irradiation reduction in the size of the spleen has rendered splenectomy easier as a preoperative measure.

Case History

Mrs. G. Enlarged spleen and liver, of three years' duration. R.B.C. 3,000,000; Hb. 70 per cent; W.B.C. 3000. Spleen to umbilicus and crest of ilium. Dec. 9, 1922, given 2400 mg.-hr. with 100 mg. radium at 1 inch distance over three splenic areas. There resulted no improvement as regards size of spleen but symptomatic and general improvement followed in six weeks.

Reference

Pinch, A. E. H. Splenic anaemia—Banti's disease. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1923. *Radium*, 3: 11, 1924.

Carcinoma of the Esophagus

Diagnosis is not discussed in this outline but should be established by roentgen-ray, biopsy and laboratory methods in every possible instance. (See p. 13.)

Pathology. The squamous-cell variety is the common type of carcinoma found in the esophagus. Its most frequent site is in the mid-portion, where there is normally a narrowing; it is less frequent at the cardia, and, rare at the level of the trachea. The lesion spreads both by linear and by annular extension. Though projection into the lumen is uncommon, the induration and thickening cause early interference with the contraction wave, with resulting rapid development of dysphagia and obstruction. Extension into the mediastinum and peribronchial lymph nodes is the rule in neglected cases. Hemorrhage, complete obstruction, perforation, mediastinitis, and gangrene are the complications which occur.

Radium Indications. While of doubtful value as a curative agent, radium therapy is almost the only nonoperative means indicated. Surgical excision is almost impossible. Radium can be applied with a fair degree of accuracy. It inhibits the growth, prolongs the life of the patient, and, together with local dilatation, renders the best available service to the patient. Complete destruction of all malignant tissue is sought but the mechanical difficulties encountered render success exceedingly difficult. No other treatment except palliative gastrostomy offers so much relief.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The type of application most commonly employed is that of the insertion of the radium capsule with beta ray screen on a semi-rigid applicator into the strictured area of the esophagus. The radium capsule may be prepared long enough to irradiate the whole linear extent of the lesion simultaneously, or a shorter capsule may be moved from segment to segment to accomplish homogeneous irradiation. Application and retention should be controlled by the fluoroscope. Should canalization of the lesion be difficult, smaller caliber applicators, using platinum filter, may be tried. If one is unsuccessful in attempts to insert a small capsule, systematic dilatation must be done, employing for this purpose a weighted thread, which, when swallowed, becomes anchored in the intestines and later serves as a guide when threaded on a small caliber bougie. Graduated soundings enlarge the lumen sufficiently to admit the radium-carrying capsule. When this latter procedure fails, a gastrostomy will be necessary if radium is to be applied accurately to the surface of the lesion. Radium applications within the esophagus, to be efficient, must be made within the involved lumen.

Other methods may be employed in the application of radium to esophageal carcinoma. The application may be made under the direct guidance of the esophagoscope, employing either cavity application or implantation of radon seeds. The capsules may be threaded on a string passing from the mouth through the esophagus and emerging from a gastrostomy fistula, but the exact placing of the radium must be controlled by the fluoroscope. Needles, too, have been inserted under the esophagoscopic control by means of a specially constructed long forceps.

With the beta ray screen the dosage may vary from 500 mg.-hr. in single applications to 1200 or 1500 mg.-hr. in series. Dosages up to 3000 or 4000 mg.-hr. are recorded, but the writer urges caution and full consciousness of the dangers of perforation, secondary hemorrhage and mediastinitis. Such dosage should be used advisedly. Gold radon seeds, 4 to 6 in number, containing 1.0 mc. to 2.0 mc. may be inserted, bearing in mind the fact that tissue 0.3 mm. in diameter is necrosed around each implant. Small platinum

needles may also be used, employing a dosage of 70 to 90 mg.-hr. per needle when they are inserted one to each cubic centimeter of tissue and with a filter allowing penetration of 5 per cent of the beta rays. Applications may be repeated in six to eight weeks.

Reaction. The general reaction is usually mild. Symptoms secondary to local changes are more often favorable than unfavorable. Immediate improvement in swallowing frequently results from simple canalization or from relief of muscle spasm, the result of the analgesic effect of the radium. For a few days the patient takes more nourishment than formerly, improves rapidly in general well-being and feels encouraged. After seven to ten days, the local inflammatory reaction becomes apparent, and dysphagia may or may not be marked. The patient may complain of a sensation of burning deep in the chest. Marked local swelling may cause dysphagia or even complete obstruction, and nutrient enemas may have to be resorted to for a few days until the local reaction subsides. The patency of the esophageal lumen may be maintained by passing bougies cautiously, guarding against trauma, especially if large doses of radiation have been given.

Locally, the reaction is that of inflammatory swelling, beginning three or four days after treatment when beta rays are employed, and from seven to ten days after the use of gamma rays only. Superficial ulceration follows shortly. Liquefaction, discharge, and sloughing follow in proportion to the dose or susceptibility of the growth. With moderate dosage the adjacent normal esophageal mucous membrane does not suffer irreparable damage. By the fourth week destructive and breaking-down processes are complete, and by the sixth week repair is usually accomplished.

Subsequent applications are indicated if bleeding and obstruction continue; if bougies carry fragments of actively growing tumor; if the esophagoscope reveals actively growing tumor; and if sounding and the fluoroscope give evidence of active growth. In any event, the radiologist is obliged to work pretty much in the dark. If from careful observation and experience the radiologist is convinced that inadequate or imperfect applications have been made or that extension has occurred, then additional irradiation is indicated.

It is possible for fatal hemorrhage to occur immediately or between five and fifteen days after treatment. Perforation with shock or rapidly developing mediastinitis, if due to traumatism, may occur immediately following the application or it may develop during the second or third week from erosion due to the destructive action of the radium. Delayed slough or slough *en masse* may occur with serious results when irradiation is heavy or an extensive growth is too rapidly destroyed.

Favorable end results should reveal a lumen but slightly narrowed, or distorted, functioning sufficiently to allow semisolid food to pass easily. If such conditions obtain six or seven weeks after treatment, immediate results may be said to be good. Fibrosis and subsequent contraction may distort or narrow the lumen, even in cases where apparent arrest of the malignant disease has been accomplished. Careful sounding, fluoroscopic examination and the use of the esophagoscope are the best means of observation at hand. Permanent local eradication of the disease is rare.

Prognosis. The immediate results are often encouraging. Dysphagia is relieved. The patient feels better as a result of lessened pain and increased consumption of food. Rapid increase in weight is common. Such improvement may last three to six months, and in a very small percentage of cases into the second or even the third year. Sooner or later, local recurrence, extension into the mediastinum, trachea, or spine, or peribronchial lymph node involvement claims the patient. Permanent cure is rarely accomplished but temporary arrest is common. In a few cases no improvement is noted. Gastrostomy is indicated when adequate radium treatment cannot be given.

Case History

Mr. C. Aged fifty-three. Carcinoma of the esophagus. Dysphagia, regurgitation, loss of weight, duration three months. Stricture at level of ninth dorsal vertebra. Dilated above. Fifty mg. radium, beta ray screen, five hours, repeated in four days. Total 500 mg.-hr. Radium passed into lumen of stricture. Immediate improvement in swallowing and general condition following ability to take food. One month later enlarged nodes appeared in neck. Decline and death in three months.

References

Beck, J. C. Discussing radium in the esophagus. *N. York M. J.*, 113: 491 1921.

Bensaude, R., and Hillemand, P. The use of a guiding thread for radium application in carcinoma of the esophagus. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 46: 703, 1922.

Carmody, T. E. Treatment of carcinoma of the esophagus with radium. *Laryngoscope*, 34: 101, 1924.

Carr, J. G., and Hanford, C. W. Carcinoma of the esophagus with perforation of the aorta. *Am. J. M. Sc.*, 164: 340, 1922.

Case, J. T. The technic of radiation therapy of esophageal carcinoma. *Am. J. Roentgenol.*, 10–859, 1923.

Fitzgibbon, J. H. Radium applicator for use in esophagus. *J. A. M. A.*, 86: 622, 1926.

Forbes, H. H. Present status of radium in laryngeal and esophageal cancer in the United States. *J. Laryng. & Otol.*, Edinb., 38: 1, 1923.

Forbes, H. H. Recent experience with radium treatment in malignant disease of the esophagus and upper respiratory tract. *Boston M. & S. J.*, 186: 705, 1922.

Frey, S. Dangers in irradiation of carcinoma of esophagus. *Zentralbl. f. Chir.*, 53: 1890–1926; abst. in *J. A. M. A.*, 87: 1344, 1926.

Greene, D. C. Treatment of carcinoma of the esophagus by radiation. *Am. J. Roentgenol.*, 12: 471, 1924.

Greene, D. C. Results of treatment of carcinoma of the esophagus by the combined use of radium emanations and deep roentgen rays. *Arch. Otolaryngol.*, 1: 51, 1925.

Guisez, J. Radium therapy of cancer of the esophagus. *Bull. d'oto-rhino-laryngol. etc.*, 20: 269, 1922.

Guisez, J. Radiotherapy of cancer of the esophagus. *Presse méd.*, 31: 193, 1923.

Guisez, J. Radium therapy in cancer of the esophagus. *Bull. d'oto-rhino-laryngol., etc.*, 21: 263, 1923.

Guisez, J. Radium therapy of cancer of the esophagus. *Bull. d'oto-rhino-laryngol. etc.*, 22: 137, 1924.

Hanford, C. W. Oesophageal radium applicator. *Surg., Gynec. & Obst.*, 31: 84, 1920.

Hanford, C. W. Radium technic in treating cancer of the esophagus. *J. A. M. A.*, 78: 10, 1922.

Herriman, F. R. Radon therapy in malignancy of larynx and esophagus. *Laryngoscope*, 37: 664, 1927.

Hill, W. Radium therapy in cancer of the esophagus. *J. Laryng. & Otol.*, 40: 73, 1925.

Hotz, G. Radium therapy in cancer of the esophagus. *Schweiz. med. Wchnschr.*, 51: 460, 1921.

Jentzer, A. Treatment of cancer of the esophagus with the automatic radium holder and its results. *J. de radiol. et d'électrol.*, 8: 529, 1924.

Kurtzahn. Radium irradiation in carcinoma of the esophagus. *Arch. f. klin. Chir.*, 121: 725, 1922.

Ledoux and Sluys. Technic of locating esophageal cancer for treatment with radium. *Arch. d'électric. méd., etc.*, 31: 353, 1923.

Ledoux and Sluys. Technic of localizing esophageal cancer for application of radium. *J. de Radiol. et d'électrol.*, 7: 549, 1923.

Lewin, C. Radium therapy in cancer of the esophagus and cardia. *Therap. d. Gegenw.*, 55: 103, 1914.

Mills, R. W., and Kimbrough, J. S. Radium treatment of cancer of the esophagus under roentgen ray control. *J. A. M. A.*, 74: 1570, 1920.

Mills, R. W., and Kimbrough, J. B. Further observations on the radium treatment of cancer of the esophagus with a review of forty-four cases so treated. *Am. J. Roentgenol.*, 10: 148, 1923.

Muir, J. Implantation of radon in esophageal cancer; description of operating esophagoscope; technique of application. *Laryngoscope*, 37: 660, 1927.

Pinch, A. E. H. Carcinoma of the esophagus. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, 2: 55, 1923.

Yankauer, S. A radium needle for the esophagoscope. *Arch. Surg.*, 6: 288, 1923.

Hodgkin's Disease

The *diagnosis* is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The essential lesion in this condition is a lymphogranuloma characterized by multiplicity of cells: endothelial, plasma cells, eosinophiles, and giant cells, with relatively few lymphocytes. The cervical nodes are most frequently involved, followed by changes in the axillary, mediastinal and retroperitoneal groups, and occasionally with splenic enlargement. It is usually a chronic disease, the enlarging glands rendering the condition serious by pressure on vital organs. Neighboring glands may be hyperplastic, but they later lose this characteristic and take on the excessive growth of various types of cells in varying proportions.

Radium Indications. Radium rays reduce the size of these massive glandular enlargements of Hodgkin's disease. This action may be due to the susceptibility of rapidly proliferating cells to the rays, or to local hyperleucocytosis, or to the alterative action of the rays. The gamma rays are suitable for penetration to the deep-seated tissues.

Few contraindications exist except possibly excessive pressure which may be increased by transient swelling of the glands, due to the radium reaction: under these circum-

stances this increased pressure constitutes a serious menace to life.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium application is made. (See p. 15.)

Application. Deep external irradiation over the lesions to the skin tolerance dosage from all possible avenues of cross-fire offers the best method of treatment. From 1000 to 1200 mg.-hr. of the gamma rays at 1 inch distance, over each 2 sq. in., may serve as a standard, safe dosage. The treatment may be repeated in from six to eight weeks if the skin reaction is mild. The total dosage may vary from a few gram-hours over isolated nodes to 30 to 50 gm.-hr. over several weeks or months in divided doses and according to the extent of involvement, evidence of delayed reduction in size, or recurrent and missed areas. Intense massive irradiation with an applicator containing from 1 to 4 gm. at 6, 10 or 15 cm. distance, probably gives the best promise of success.

Reaction. The general reaction, which may be marked after the administration of 5 or more gram-hours, is characterized by malaise, anorexia, headache, nausea, occasionally vomiting, and not infrequently a rise in temperature. It often begins while the application is still in progress as a direct result of the radiation on the general body tissue. It may continue temporarily from the direct effect of the rays.

The secondary reaction, due to the local changes within the lesion, begins within from five to ten days. Cells are rapidly destroyed and absorbed. This absorption, which is manifested by a decrease in the size of the irradiated masses, causes further general intoxication, resulting in the continuous general reaction. By the fifth week the general reaction usually subsides. There is but little change in the blood picture unless a dosage of many gram-hours is given within a few days. Locally, there is noted within a few days swelling of the lesions, followed by shrinking beginning as early as the tenth day and continuing often for three weeks or more. Intensely cellular masses yield more rapidly and to a greater extent than chronic lesions with fibrosis and relatively decreased cellular content. The shrinkage

of the masses has usually reached its maximum by the fifth or sixth week. Complete disappearance of nodes may not be accomplished, due to the remnant of the framework of the glands. A benign nodule may persist permanently. Many nodes of long standing shrink only moderately, yet sufficiently to relieve the pressure caused by them.

Recurrences may appear in adjacent or distant chains of nodes but they are not so likely to recur in well-irradiated areas. The depths of the nodes receive less irradiation than the surface unless one employs large amounts of radium at 10 to 15 cm. distance. If there is not sufficient irradiation, by crossfire, these deep areas may be the site of recurrence. Favorable cases terminate with marked reduction of lymphogranulomatous masses to the extent of no longer giving serious pressure symptoms. Recurrences elsewhere in the body may appear within a few months to be subjected to irradiation again. Eventually in practically all cases, masses reappear from new nodes or from the remnants of those formerly involved and most patients with this disease finally succumb.

Prognosis. Practically all lesions of Hodgkin's disease yield more or less completely to efficient radium irradiation, at least temporarily. In a few months other areas are involved which may yield, and this process may be repeated until some inaccessible or unyielding mass encroaches upon vital structures or toxemia of long standing eventually claims the patient. Palliative treatment with radium is of hopeful value; even occasional lasting cures have been reported.

Case History

Mrs. H. Hodgkin's disease. Nodules in cervical, axillary and inguinal nodes with increased dulness in chest and shadows under roentgen-ray examination. W.B.C. 30,000; R.B.C. 4,500,000; Hb. 70 per cent. General weakness. Between March 1 and 11, the patient was given 12,000 mg.-hr. of radium, using 100 mg. at 1 inch distance over the enlarged nodes and over the mediastinum. There was immediate relief from pain and general improvement continuing for two years.

Refereces

Aikins, W. H. B. The use of radium in the treatment of the leukemias and Hodgkin's disease. *Am. J. Roentgenol.*, 10: 853, 1923.

Bowing, H. H. The value of radium and x-ray therapy in Hodgkin's disease. *J. Radiol.*, 2: 20, 1921.
Desjardins, A. U. The radiation treatment of Hodgkin's disease with particular reference to mediastinal involvement. *Radiology*, 1: 161, 1923.
Desjardins, A. U., and Ford, F. A. Hodgkin's disease and lymphosarcoma. *J. A. M. A.*, 81: 925, 1923.
Levin, I. X-ray and radium treatment of leukemia. *Med. & Surg.*, 1: 411, 1917.
Schreiner, B. F., and Mattick, W. L. Radiation therapy in forty-six cases of lymphogranuloma (Hodgkin's disease). *Am. J. Roentgenol.*, 12: 133, 1924.

Hyperthyroidism

The *diagnosis* is not discussed in this outline but should be established by estimations of basal metabolic rate and the usual clinical and other laboratory tests. (See p. 13.)

Pathology. In toxic goiter the glandular elements are hyperplastic and hypertrophic with an increased vascularity and a decrease in colloid formation. Cuboidal and columnar cells replace the normal pavement epithelium and there is marked increase in the secretion of the thyroid hormone due to a stimulus of toxic or other origin. The hyperplasia may be found general, parenchymatous or localized in areas, and associated with decrease in colloids. Not uncommonly the condition is complicated by an hypertrophied thymus. There is an increased metabolic rate. Later in the course, hypoplasia may follow with an increase in connective tissue and with atrophy of the hyperactive cells. This decreased function may continue even to hypothyroidism in untreated cases. The increased secretion of the hormone, if uncontrolled, leads to secondary cardiac, nervous system, digestive system, and general metabolic disturbances. Unrestricted, uncontrolled hypertrophic and hyperplastic goiters are fatal through general toxemia from increased hormone secretion.

Radium Indications. It has been repeatedly demonstrated that radium radiation is able to reduce the action of exophthalmic goiter, as evidenced by reduced basal metabolic rate and subsidence of the toxic symptoms. The hard gamma rays possess a degree of penetration which reaches the depth of the gland and is unequaled by any other type of radiation. Theoretically the hyperplastic cells are susceptible to the rays; this special susceptibility may account for the results obtained. Or the favorable result may be due to the

tendency of radiation to reduce blood supply by obliterative endarteritis. Subsequent increased connective-tissue formation, not unlike that found in spontaneously cured cases, may also be a factor in the reduction of toxicity because of the contraction of the connective tissue and resulting restriction of hyperfunction. Extremely toxic individuals in a serious condition may be temporarily thrown into a frenzy by the transient increase in all symptoms which follows radium irradiation. Such cases should be given small doses if they are to be treated at all. The hard gamma rays are the ones principally employed in the treatment of hyperthyroidism.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium application is made. (See p. 15.)

Application. Deep external irradiation with the gamma rays over both lobes and the isthmus, to the extent of 1500 to 3000 mg.-hr. at 1 inch distance in divided doses, expresses a fair dosage of radium in exophthalmic goiter. Dosages as low as 500 and as high as 5000 mg.-hr. in divided doses and repeated treatments over many months may represent the two extremes in dosage. Surface treatment has no useful place in goiter therapy. The interstitial method may be used with success in the form of needles of radium element or radon implants, placed within the gland through a skin incision to be sure the applicators are lodged within the pathological tissue. The object of interstitial applications is to destroy permanently areas of the thyroid for a radius of 0.5 cm. about each applicator. The dosage consists of 1 mc. gold implants or 75 to 130 mg.-hr. per needle. Complete destruction of the gland must be avoided. The number of implants or needles used depends upon the size of the gland and the degree of toxicity. Roentgen examination of the thymus should be made prior to treatment; and, if this organ is pathologically enlarged, irradiation over the sternum to the extent of 1000 to 1200 mg.-hr. of gamma radiation at 1 inch distance over each 2 sq. in. of skin surface may serve as a safe dosage covering one or two areas. The initial dose over the thyroid may vary from 100 to 500 mg.-hr. inversely according to the degree of toxicity. The second dose, given

one week later, may be increased to double the initial dose; and the third, one week later, may be double or treble the initial dose according to the severity of the reactions to the previous treatment. The less toxic and the less serious the condition, the more rapidly may the treatments be given without untoward effect. Dosage depends on the severity of the case, the stage of the disease, its acuteness or chronicity, the available radium and the previous practices and personal equation of the radium therapist. In cases of questionable diagnosis of hyperthyroidism an initial dose of 500 mg.-hr. elicits no reaction, while in toxic goiter an increase of symptoms can frequently be noted in mild degrees of hyperthyroidism. This reaction suggests the possibility of a therapeutic test.

Reaction. Within thirty-six hours, in marked degrees of hyperthyroidism, there occurs a general reaction characterized by increased pulse rate, accentuated nervous phenomena, tremor, insomnia and increased metabolic rate, resembling an acute exacerbation of the disease. Ordinarily, if not too severe, these symptoms subside in from three to five days, so that at the end of seven days the general condition may be slightly improved as compared with the initial symptoms. The second application may then be given, greater in amount if the reaction was mild, the same in amount if the reaction was severe or prolonged. The second reaction resembles the first. The third treatment one week later is ordinarily a repetition of the others in respect to reaction. Two of the reactions may be mild, while the one associated with thymus irradiation may be much more marked than the other two. The interstitial dose is given at one sitting and results usually in a reaction much more violent than any other and of longer duration. Single external irradiation doses may be followed by severe reaction, lasting two to four weeks, with subsequent gradual subsidence of symptoms.

From two to four weeks after the completion of the radium treatment, the general condition is often about the same as at the outset. Then follows a gradual decline of the metabolic rate, loss of nervousness and mental excitability, some decrease in pulse rate, a return of appetite, increased

ability to sleep and gradual gain in weight in patients who have lost a great deal of weight. At the end of three to six months, under efficient treatment, few evidences of symptoms remain; there has been a gain in weight, and a return of the general well-being of the patient. Tachycardia and exophthalmos are the last symptoms to yield.

If at the end of six months evidences of hyperthyroidism are still present, renewed treatment is indicated.

Seriously ill patients should be treated in the hospital, with careful medical supervision during and following the irradiation. Mild cases may be ambulatory. Acute cases and those of long standing with marked secondary pathology require careful conservative irradiation on account of the possibility of an acute exacerbation of symptoms in acute cases, too great to endure, and of too sudden removal of the excess of hormone in chronic cases long accustomed to hypersecretion. Conservatism in therapeutic dosage with the employment of divided doses is probably the safest procedure in serious cases. Mild degrees of thyroid intoxication may be more vigorously and rapidly irradiated with relative safety.

Locally the reaction is mild or absent on the skin. However, the skin of the neck in exophthalmic goiter patients is unusually susceptible to irradiation. Vascular phenomena of an erythematous nature may occur within a few days but it is not the erythema of normal skin reaction, either in character or time of appearance. This erythema seems to be a transient, vasomotor disturbance, synchronous with general reaction, and is sometimes accompanied by a slight swelling or puffiness in the thyroid gland itself. The distance employed and in general the skin dosage are best kept well below the erythema dose on account of the apparent skin susceptibility in this disease. No marked change in the size of the gland is observed, either as to swelling or subsequent shrinkage.

Favorable cases return to normal metabolic rate, appetite, ability to work and sleep, with a normal pulse rate if the case is not of long standing. In chronic cases the pulse rate and exophthalmos may yield very gradually. The damage done to the myocardium may never be entirely

cradicated. Exophthalmos may persist indefinitely. Unfavorable cases may occasionally be thrown into an acute exacerbation from which they do not recover. Other cases may be resistant and the symptoms persist in spite of all effort. The reaction, in general, depends to a large extent on the stage in the clinical course of the disease, on the adjustment of the dosage to the individual case and on accurate control of post-irradiation treatment in general.

Prognosis. A large majority of toxic goiters are improved by radium treatment. This improvement varies from slight lowering of the metabolic rate and abatement of symptoms to apparent clinical cures, lasting for months and years. A few extremely toxic cases suffer a serious exacerbation from which recovery may not occur. The majority of exophthalmic goiters may be improved or cured by careful irradiation. It is not radical to state that radium is a valuable aid in the general management of toxic goiter, and it could well be employed to a much greater extent than it now is.

Case History

Mrs. W. Goiter. Nervousness, tremor, tachycardia, occasional diarrhea, loss of weight, metabolic rate +92. Over ten days patient was given 2400 mg.-hr. radium with 50 mg. irradiating both lobes and isthmus as well as the thymus area. Improvement was gradual, steady, to normal in six months, and cure has continued for five years.

References

Aikins, W. H. B. Exophthalmic goiter with special reference to the etiology and treatment with radium. *New York M. J.*, 104: 49, 1916.

Aikins, W. H. B. Radium in toxic goiter. *Canad. Prac. & Rev.*, 45: 339, 1920. 1920.

Bower, J. O., and Clark, J. H. A Preliminary report of the action of buried radium on diseased thyroids in man. *Am. J. Roentgenol.*, 10: 875, 1923.

Grier, G. W. X-ray and radium treatment of goiter. *Atlantic M. J.*, 26: 516, 1923.

Gudzent, F. The effect of small doses of rays (radium and mesothorium) on thyrotoxicosis and Basedow's disease. *Klin. Wchnschr.*, 3: 2329, 1924.

Hagans, F. M. Radium therapy of goiter. *Internat. J. Med. & Surg.*, 37: 151, 1924. *Endocrinology*, 8: 404, 1924.

Heyerdahl, S. A. Radium treatment of changes in the thyroid gland. *Acta Radiol.*, 1: 207, 1921.

Holmes, G. W. Radiation therapy of the thyroid and ductless glands. *Boston M. & S. J.*, 191: 10, 1924.

Loucks, R. E. Pathologic classification of thyroid gland diseases with radium treatment in toxic goiter. *Am. J. Roentgenol.*, 8: 755, 1921.

Loucks, R. E. Radium treatment of toxic goiter with metabolic deductions. *Am. J. Roentgenol.*, 10: 767, 1923.

Loucks, R. E. Radium treatment of thyrotoxicosis. *Radiology*, 4: 473, 1925.

Pinch, A. E. H. Exophthalmic Goiter. A Report of the Work at the Radium Institute, London, from January 1, 1923 to December 31, 1923. *Radium*, 3: 7, 1924.

Skinner, E. H., and Lockwood, I. H. Radiotherapy of goiter. *J. Missouri M. A.*, 23: 11, 1926.

Stevens, J. T. Toxic goiter; its treatment by means of radium and roentgen rays; results controlled with basal metabolism. *Radiology*, 6: 7, 1926.

Swanberg, H. The radiation treatment of hyperthyroidism and the basal metabolism test. *J. Iowa M. Soc.*, 12: 442, 1922.

Leucemia (lymphatic, acute and chronic)

Diagnosis is not discussed in this outline but should be established by laboratory findings in every possible instance. (See p. 13).

Pathology. The disease, which is progressive and invariably fatal from the associated toxemia or anemia, is characterized by hyperplasia of the lymphoid tissues, especially the cervical, axillary, and inguinal glands, with excess of lymphocytes in the blood stream. Often the spleen partakes of the enlargement, either as a protective agent or because of cellular hyperplasia in this organ. The disease may be acute, the common form in young people, or chronic, the ordinary type seen in later life. The acute form runs a rapid course in a few days or at the longest a few weeks with a fatal termination. The chronic form may run a course of several months to two or three years.

Radium Indications. Radium irradiation has frequently been demonstrated as a powerful agent to lower the white blood cell count and to cause marked decrease in the involved lymph glands and the spleen with relatively little deleterious effect upon the erythrocyte count. The treatment and observations are relatively simple. There is little danger except in the fulminating, acute lymphatic type, in those conditions where the hemoglobin is below 50 per cent, and during treatment when the leucocyte count falls far below normal. Radium rays destroy in large numbers the

rapidly forming lymphocytes within the glandular substance and in the blood stream. It is probably a destruction rather than a withdrawal of the cells to recesses in the body which occurs as a reaction to irradiation.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation over the enlarged lymph nodes and the spleen with cross-fire wherever possible is the method of choice in treating lymphatic leucemia.

From 1000 to 1200 mg.-hr. of gamma rays at 1 inch distance over areas, each 2 sq. in. of skin surface, is a safe dosage in the chronic type of the disease. The spleen when palpable should be irradiated. The total dosage over a period of ten days may amount to 10 to 20 gm.-hr. safely in the chronic form with mild anemia.

Acute lymphatic leucemia is much more difficult to treat. Moderate dosage of 1 gm.-hr. per treatment, probably best given on alternate days, with careful check-up on blood counts, temperature, and general reaction has proved to be a fairly safe procedure. When the leucocyte count approaches normal the treatment should be suspended.

In chronic types treatment may be repeated in six to eight weeks but ordinarily the remission lasts longer. The reenlargement of nodes or the appearance of enlargement in new chains, together with elevation of the white cell count, indicate re-treatment. The dosage in the second series should be lighter than in the first, with reduced dosage per area in parts previously treated. The total irradiation in the second series had better be reduced to 5 or 10 gm.-hr., depending on the local conditions, the white cell count and the general condition of the patient.

The acute type responds quickly but is followed by a very prompt recurrence of the elevated leucocyte count, the swelling of the lymphoid tissue and the general asthenic state of the patient. Re-treatment may safely be given in 1 gm.-hr. doses, when the leucocyte count rises to 25,000 or thereabouts, and swelling in the nodes and spleen reappears. Repeated doses and the intervals between them must be conservatively adjusted to the general condition of the patient.

Reaction. In chronic lymphatic leucemia, the more common type, the general reaction is usually not severe. Malaise, anorexia, with some headache and slight rise in temperature, ordinarily comprise the general reaction. Dosage of from 1 to 2 gm.-hr. per day in patients in fair general condition results in no untoward effects. The malaise with some loss of weight may continue from three to four weeks after the irradiation and longer in debilitated patients. Anemia may be slightly increased, although usually not markedly so.

In the acute type general weakness is marked, and there is danger of sudden collapse, either due to the disease or to the treatment. Careful administration of 1 gm.-hr. dosage, two or three times per week, is not usually associated with any marked general reaction. Dosage amounting to 2 gm.-hr. each day is liable to result in a rapidly falling white cell count, fever and marked prostration. Blood transfusion is indicated in prostration with marked anemia or in white cell counts going below 3500, especially if there has been considerable rapid drop in the count. Supportive measures of a general medical nature under hospital management are imperative. A daily check of the blood picture is required.

Locally the involved nodes and spleen show a reduction in size within a few days after the treatment is begun. The white cell count falls from 10,000 to 20,000 per day, often to normal in from ten to twelve days. The spleen and nodes are reduced to a stationary minimum in three or four weeks. In the acute type the nodes and spleen yield rapidly although with a lesser degree of certainty than in the chronic type. The white blood cell count may fall rapidly and may go to 3000 or even lower. White cell counts below 3500 are danger signals, revealing the serious menace of a sudden collapse and a fatal outcome. In this type recurrence is prompt and marked. When it occurs, the leucocyte count may reach its original level or much higher within a few days after the cessation of treatment. Nodal and splenic enlargement accompany the rising blood count. General weakness gradually increases. At best the fatal outcome too often follows within a few weeks.

In chronic types favorable cases show a return to the normal white cell count and the reduction of glandular enlargement to a symptomless minimum. This condition of well-being lasts for a variable number of months until recurrences finally appear and the original condition obtains coincident with other glandular changes and a mounting white cell count. Re-treatment is indicated. The second series of treatments yields results comparable to the first, but in lesser degree. Again recurrences appear and treatment again improves the condition, until anemia, toxemia, or the reaction to the treatment overwhelms the patient. Such remissions occur without any treatment but improvement can be produced almost at will with efficient radium treatment. In the end all acute and chronic lymphatic leucemia cases terminate fatally.

Prognosis. It is safe to say that the average case of chronic lymphatic leucemia is markedly improved symptomatically by efficient radium treatment; that relative comfort is temporarily restored; that life is prolonged; and that the treatment with radium is justified and well worth while.

Acute lymphatic leucemia is a rapidly fatal disease, which may be delayed briefly in its course by radium treatment, but not without risk of hastening the end through the reaction to the radium or by producing a sudden collapse due to secondary toxemia from the destroyed lymphoid tissue.

Case History

Mr. P. Aged twenty-three. Acute lymphatic leucemia. Weakness with prominence of abdomen for six weeks. Glandular swelling in neck. Spleen enlarged to umbilicus. Liver enlarged. Axillary, cervical, and inguinal adenitis. W.B.C. 118,000; R.B.C. 3,800,000; Hb. 55 per cent. Treatment consisting of 9960 mg.-hr. radium over spleen, liver and enlarged glands, using not more than 50 mg. radium at one time. Duration of treatment, fourteen days. Beta ray screen, 1 inch distance. W.B.C. in four days, 13,000. In ten days, liver, spleen, and glands decreased in size. In ten days W.B.C. increased again to 50,000. More radium therapy. Leucocytes down to 3200, but immediately rose to 210,000 by twenty-fifth day. Severe nosebleed, coma, and death on twenty-eighth day.

References

Knudson, A., and Erdos, T. Metabolism study of a case of leukemia during radium treatment. *Boston M. & S. J.*, 176: 503, 1917.

Minot and Isaacs. Lymphatic leukemia; age incidence, duration, and benefit, derived from irradiation. *Boston M. & S. J.*, 191: 1, 1924.
Brown, W. L. Radium therapy of leukemia. *Am. J. Roentgenol.*, 19: 15, 1928.
Tomanek, F. Results in prolonged radium therapy of leukemia. *Strahlentherapie*, 25: 694, 1927.

Leucemia (myelogenous)

Diagnosis is not discussed in this outline but should be established by all laboratory and clinical tests possible. (See p. 13.)

Pathology. This condition is characterized essentially by an abnormal hyperplasia of the blood-forming organs, chiefly the bone marrow. The excessive formation of polymorphonuclear leucocytes with a preponderance of myelocytes in the blood stream is characteristic. The leucocyte count may vary from a few thousands to a million. There is an accompanying increased formation of red cells also. Anemia, weakness, and faulty circulation follow the choking of the smaller vessels with the white blood cells. The spleen is greatly enlarged, either because of its action as a filter or to provide for the excessive formation of cells, or both. The organ may be enormous. The condition is usually chronic, lasting from a few months to a few years and is invariably fatal.

Radium Indications. The penetrating rays of radium destroy white blood cells. This is shown by examination of blood smears and by the marked decrease in the leucocyte count, and general improvement in the patient's health, repeatedly seen as an accompaniment of this destruction. The application is relatively simple and carries with it a minimum of danger.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation may be administered over the enlarged spleen to the extent of 1000 to 1200 mg.-hr. of gamma radiation at 1 inch distance over areas each including 2 sq. in. of skin surface. The average dose varies between 5 and 10 gm.-hr. This usually brings the white cell count down to normal. The spleen shrinks markedly. The long bones also may be irradiated. Treatment of

the long bones rather than of the spleen, when the spleen is enlarged, is of less value than irradiation over that organ. Re-treatment in three to twelve months is indicated depending upon the rapidity of reappearance of leucocytosis and splenic enlargement. A second series of applications resembling the initial treatment may be administered, and similar improvement expected; but there will be a subsequent reappearance of symptoms.

Reaction. The general reaction may be marked when using dosages of from 6 to 10 gm.-hr., characterized by malaise, anorexia, headache, occasional nausea and vomiting. It begins during the treatment and lasts for a few days. The general depression may persist from two to four weeks, rarely longer. Locally, the spleen may temporarily increase in size, but it shrinks from 50 to 80 per cent within eighteen or twenty days. The white cell count may drop 100,000 or more per twenty-four hours, until a fairly low count is reached. Fragments of disintegrating myelocytes may be seen in numbers in the blood smears of specimens taken during the first two or three days of efficient treatment. The count is often reduced to 10,000 or 20,000 within ten days, and may gradually fall to normal within three or four weeks. It may remain stationary for many months. After the general reaction subsides, the anemia improves, the blood count often returning to normal, and the general health may approach the normal enjoyed previously by the individual. Second treatments are followed by the same results to a lesser extent in all respects. The spleen is never reduced to its normal size, the white cell count falls more gradually and not so completely. The red blood picture improves but not quite so much. The third series of treatments is accompanied by still less satisfactory results, until eventually the patient succumbs to the disease. Most favorable cases obtain a fair degree of palliation and increased comfort with a probable prolongation of life. Advanced cases and patients weakened at the outset do not do so well.

Prognosis. All patients with myelogenous leucemia die of the disease. Radium therapy probably relieves suffering and prolongs life. It is true that many untreated cases have

remissions, but the regularity with which the blood picture, the splenic enlargement, and the general health can be repeatedly improved, indicates that radium as a palliative measure is a valuable agent in this eventually hopeless condition.

Case History

Mr. F. Myelogenous leucemia. Felt below par and consulted a physician who found a palpable spleen and W.B.C. 179,000. No other abnormalities. A total of 7200 mg.-hr., in divided doses, at 1 inch distance over the spleen with beta ray screen, was given, during a period of six weeks, using 50 mg. radium. At the end of six months the W.B.C. count was 6000 and the patient otherwise normal. Lived in comparatively good health until he finally succumbed to a recurrence after thirty-two months.

References

Bigger, I. A. Jr. The radium treatment of chronic myelogenous leukemia, with a report of five cases. *Virginia M. Monthly*, 50: 543, 1923.

Bonta, M. B. Radium in the treatment of leukemia. *Ann. Clin. Med.*, 1: 155, 1922.

Bower, J. O., and Clark, J. H. Two cases of myeloid leukemia complicated with pregnancy treated with topical applications of radium. *Am. J. Obst. & Gynec.*, 9: 207, 1925.

Burg, K. M. A case of myeloid leukemia. *Deutsch. Med. Wchnschr.*, 50: 881, 1924.

Giffin, H. Z. Observations on the treatment of myelocytic leukemia by radium. *Boston M. & S. J.*, 177: 686, 1917.

Henriques, A., and Menville, L. J. Radium in the treatment of myelogenous leukemia. *New Orleans M. & S. J.*, 75: 247, 1922.

Minot, G. R., Buckman, T. E. and Isaacs, R. Chronic myelogenous leukemia. *J. A. M. A.*, 82: 1489, 1924.

Ordway, T. Remissions in leukemia produced by radium in cases completely resistant to x-ray and benzol treatment. *Boston M. & S. J.*, 176: 490, 1917.

Peabody, F. W. Report on the treatment of myelogenous leukemia with radium. *Boston M. & S. J.*, 177: 873, 1917.

Schreiner, B. F., and Mattick, W. L. Radiation therapy in treatment of leukemias. *Am. J. Roentgenol.* 12: 126, 1924.

Whitcher, B. R. Blood changes in myelogenous leukemia following radium treatment. *Boston M. & S. J.*, 187: 349, 1922.

Neurofibroma (von recklinghausen's disease)

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Neurofibroma, usually multiple in character, originates in the peripheral nerves and is composed of fibrous

tissue overgrowth along the course of the nerves, frequently at the nerve endings. The condition is extensive and may eventually involve all the peripheral nerves and even the central nervous system. Hyperesthesia and real pain usually accompany the tumors. Under the skin of these patients can be felt hundreds of small tumors, varying in size from a few millimeters to many centimeters in diameter. The disease is progressive, non-limited, and incurable.

Radium Indications. Radium rays may be employed as a palliative in this condition for the purpose of reducing the hyperesthesia and pain. In an incurable chronic condition, such as neurofibromatosis, the relief of pain and hyperesthesia becomes a serious problem.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation is practically the only method available in the radium therapy of this condition. The dosage is light, the application simple; there should be no skin reaction, and the applications may be repeated many times if necessary to control the hyperesthesia and pain. From 200 to 500 mg.-hr. of gamma radiation at 1 inch distance over each 2 sq. in. of surface of involved areas will serve to relieve the troublesome symptoms.

Reaction. There is no general reaction. Locally, the pain and hyperesthesia, if amenable at all to the radiation, will be relieved within thirty-six to forty-eight hours after treatment. This relief from pain and hyperesthesia endures for several weeks or months at least. In one instance the relief has continued for one year in areas efficiently irradiated. In one known instance the tumor masses under the skin became smaller and disappeared within three or four weeks after external irradiation, and did not recur *in situ*.

Prognosis. In von Recklinghausen's disease, a hopeless condition, radium should be used in the hope of controlling the pain and hyperesthesia. The fibrous nature of the tumors would indicate that they might possibly shrink and disappear as do keloids with the subsequent replacement of the dense fibrous masses by a fine, pliable connective tissue which causes no symptoms. Any agent which offers the

least hope of symptomatic relief and gives some promise of real destruction of pathological tissues should certainly be employed in this hitherto hopeless condition.

Case History

Master O. Aged eight. Subcutaneous nodules, varying in size from millet seed to 2 cm. diameter, located in two general areas, one over the seventh cervical vertebra and the other centering over the lumbosacral junction. Nodules very numerous, covering an area 10 inches in diameter at the cervical region and 18 inches in the sacral region. Dark pigmentation, with exeessive hair and extreme tenderness over affected area. Unable to bear the contact of elothes and slight pressure against lesions. Backward in school. Sleeps only a few hours at a time. Duration of trouble, four years, increase in area of involved regions and in intensity. Over a period of three years, the patient has been given approximately 20,000 mg.-hr. of radium with beta ray screen at 1 inch distance over areas eaeh ineluding 2 sq. in. of skin surface, but never more than 500 mg.-hr. per area at a single treatment. No hyperesthesia since first treatment. Nodules began to shrink after first irradiation. Repeated treatments have caused complete disappearance of lesions about thorax. There are still many isolated nodules here and there over the body, but general health greatly improved during the three and one-half years since radium therapy began.

Thymus (enlarged)

Diagnosis is not discusssed in this outline but should be assured by roentgen-ray and clinical study in every instance. (See p. 13.)

Pathology. In this group is included chiefly the thymus gland of infancy, which undergoes hypertrophy sufficient to cause symptoms by pressure on the trachea and the large vessels of the mediastinum, the principal symptom being interference with respiration. Instead of an organ weighing a few grams and clinically not discernible the gland is many times enlarged by lymphoid hyperplasia or proliferation, resulting in a clinically distinguishable organ, giving mechanical symptoms and easily demonstrated by the roentgenogram. Not all cases are fatal, but the mortality in untreated, enlarged thymus is high, and the menace to the patient is great. Untreated cases are not infrequently later associated with status lymphaticus and its often fatal outcome.

Radium Indications. The gamma rays of radium have almost a specific action upon the enlarged thymus. The

application is simple and without danger. Permanent cure in a high percentage of the cases has been demonstrated. Complete atrophy of the hyperplastic and proliferating lymphoid tissue occurs in almost all cases when adequate radium treatment has been administered.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation over the gland anteriorly is the only available method of treatment. From 600 to 1200 mg.-hr., employing as much radium or radon as is available in one exposure, usually suffices. The distance of from ¾ to 1 inch from the skin to the beta ray screen should be maintained to prevent skin reaction. One hundred milligrams placed over each of 4 areas of 2 sq. in. for a total of 1000 mg.-hr. at ¾ inch distance is a safe standard of technic. Second applications are rarely necessary.

Reaction. The general reaction is mild or absent. Locally, shrinkage begins within a few days, probably due to the extreme susceptibility of lymphoid tissue. Symptomatic relief, characterized by disappearance of dyspnea, may be apparent within forty-eight hours. Complete atrophy with clinically and roentgenologically negative findings is usually accomplished within three or four weeks. No complications or untoward effects have been noted. Recurrences do not appear.

Prognosis. Practically all cases of abnormally enlarged thymus gland in infants yield promptly and completely to 1000 mg.-hr. of properly applied, deep external radium irradiation.

References

Brayton, H. W., and Heublein, A. C. Enlarged thymus gland in infancy and its treatment by radium. *Boston M. & S. J.*, 181: 740, 1919.

Drea, F. W. The enlarged thymus gland. *J. Radiol.*, 5: 193, 1924.

Grier, G. W. The diagnosis and treatment of enlarged thymus. *Am. J. Roentgenol.*, 11: 141, 1924.

Heublein, A. C. Radium treatment of enlarged thymus glands in infants. *Am. J. Roentgenol.*, 7: 191, 1920.

Janeway, H. H. The treatment of malignant tumors of the thymus gland by radium. *Ann. Surg.*, 71: 460, 1920.

Pfahler, G. E. The diagnosis of enlarged thymus by the x-ray and treatment by x-ray or radium. *Arch. Pediat.*, 41: 39, 1924.

PART III

GYNECOLOGICAL DISEASES

Caruncle of the Urethra

Diagnosis is not discussed in this outline, but should be established by biopsy if it seems desirable. (See p. 13.)

Pathology. This lesion is a papillomatous, vascular, almost hemangiomatous, hypertrophic lesion of the female urethra. It may be papular, pedunculated, or sessile in form. The common site is the inferior surface of the urethra, forming a crescent about the meatus. The lesion extends from 1 to 3 cm. along the floor of the canal. It is sensitive, frequently bleeds, causes pain and irritation, results in frequent micturition, and not uncommonly renders life almost unbearable. The lesion is chronic in type and occurs most often in middle adult life, rarely in young women. The etiologic factor is probably irritation from pathology higher up in the genitourinary tract. It is believed to be a forerunner of the rare carcinoma of the urethra.

Radium Indications. Radium irradiation is suitable for the destruction of vascular hypertrophic excrescences such as caruncles. Radium has repeatedly demonstrated its ability to destroy these lesions. Obliteration of small vessels and necrosis or atrophy produced within the susceptible hypertrophic tissues are the factors utilized in the radium treatment of this lesion. There are no contraindications to radium therapy, provided local pyogenic infection can be ruled out. Caruncles in young girls and nulliparous patients seem to offer a special problem. The radium treatment of these lesions in young women is attended by complications and sequelae which arouse doubt as to the advisability of its use in this class of women. Inability to bear the reaction is marked in young women as compared with mature multiparous patients. A hypersensitiveness which persists for months, together with a greater tendency to recurrence in young women, necessitates the utmost effort to eradicate the lesion by other general and local measures before subjecting these patients to radium treatment. When radium is used, heavy screening is advisable.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Cavity, surface, and interstitial methods of application are available for the treatment of urethral caruncles. A combination of the three probably offers the best results. A beta ray screened capsule in the urethral canal extending the length of the lesion, together with radium element needles, employing 10 to 15 per cent of the beta rays, inserted parallel to the urethral canal with a flat applicator against the meatus, employing from 10 to 15 per cent of the beta rays, furnish complete irradiation and cross-fire reaching all parts of the lesion. The dosage *in toto* may vary from 150 to 500 mg.-hr. The needles may be standard 12.5 mg. needles or smaller in content, placed 0.5 cm. from the canal and delivering from 100 to 200 mg.-hr. The capsule in the canal may deliver from 50 to 100 mg.-hr. Flat full-strength applicators, placed against the meatus, screened to transmit 10 to 15 per cent of the beta rays for from one to two hours may be used. Heavier intraurethral doses, plus the surface treatment over the meatus, may be successful in superficial early lesions. In general, the interstitial use of needles or gold implants surrounding the lesion is attended with a higher degree of success. Surface treatment alone is usually inadequate. Treatments may be repeated in six to eight weeks. However, the effort should be made to render the initial dose adequate. Missed areas, incompletely eradicated lesions, and recurrences may be retreated after six or eight weeks, keeping in mind the increased fibrosis, the decreased blood supply, and the liability of the tissues to slough. The second dose should be smaller, and especial effort should be made accurately and adequately to irradiate only the lesion itself, avoiding as far as possible the recovered and uninvolved tissues. Local anesthesia suffices for making the application. Interlabial packs with temporary suture through the labia majora or adequate adhesive strapping and *T*-binder retention may be sufficient. The labia should be packed as far away from the radium as possible during the application. A third application is rarely advisable.

Reaction. The general reaction is mild or absent. Locally the reaction is often severe and troublesome. As a rule, inflammatory swelling begins within a week. Redness, swelling, pain, and superficial ulceration in surface and cavity application alone often constitute a mild local reaction without urethral ulceration. By the fifth week the local inflammation has subsided, and pallor, atrophy, and fibrosis are in evidence. During the height of the inflammatory reaction, local itching, burning, and pain may be severe, requiring sedatives, bland local applications, and much encouraging of the patient. Middle-aged women often complain but little. Young women occasionally suffer severely from the local reaction and subsequent hyperesthesia which may persist for months. Rarely necrosis about the needle may produce sterile abscesses with swelling and subsequent sinus formation requiring incision for drainage of accumulated debris. In all instances, healing is complete by the sixth week or earlier. The frequent micturition subsides and in favorable cases complete relief is the result.

Recurrences may appear within six months, rarely later. In unfavorable cases, recurrence or incomplete destruction is in evidence by the sixth week. When re-treatment is indicated, it should be given with extreme care. Third treatments are inadvisable. Hyperesthesia in young women is commonly present and may persist for months, especially in cases of many years' standing. The local lesion may even be eradicated but the symptoms persist.

Prognosis. Radium therapy of urethral caruncle in middle-aged patients is attended with a high percentage of excellent results. Recurrences are uncommon after six months. In young women the local eradication, though often accomplished, may not be attended with a corresponding abatement of the symptoms. All probable etiologic factors in the genitourinary tract should be eliminated before caruncles are subjected to radium treatment.

Case History

Mrs. M. Caruncle. Red, raised, soft, puffy, ulcerated mass surrounding urinary meatus. Present for four years with little change. Microscopic diagno-

sis: benign. Extending about ½ inch back along floor of urethra, 50 mg. radium for five and three-quarter hours. One tube 12.5 mg. in urethra, three 12.5 mg. needles to right, left, and inferior to urethral canal, and parallel to it. Clinically cured for two years.

Chorioepithelioma

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. In its virulent form this neoplasm is one of the most rapidly destructive and fatal of malignant growths. The onset usually follows abortion and is characterized by a wide growth of syncytial cells and also of the cells of the Langhans layer. Cell growth is rapid without independent blood supply and without encapsulation. The growth is greater in the lumen of vessels than in the uterine sinuses. Destruction of the uterine wall and metastasis to pelvic structures is common. Frequently the lung is the site of secondary lesions. Hemorrhage, infection, and putrefaction frequently accompany the growth. The peritoneal surface of the uterus, the Fallopian tubes and the vagina are early sites of growth. In the more malignant types, excessive bleeding and cachexia put an end to the patient within a few months. Erosion and invasion of the uterine wall occur in beginning moles of non-malignant character. Chorioepithelioma is a malignant neoplasm, almost invariably causing death within a few months.

Radium Indications. Radium irradiation is suitable for the destruction of the rapidly proliferating cells of chorioepithelioma. Embryonic cells succumb to radium rays more readily than do normal structures. Mechanical disturbance and the danger of promoting embolic spread are reduced to a minimum by the employment of radium therapy. Application of radium following curettage for diagnosis is attended with but little additional trauma. The dosage must be heavy if all malignant cells within the organ are to be reached. The danger of infection and putrefaction constitute the chief obstacles to the use of radium; the greatest danger in the treatment of this condition lies in the traumatic dissemination of the growth. Radium treatment is accompanied by the least trauma of any mechanical method of treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The intrauterine application of beta ray screened radium until the tolerance dose has been administered is urgently indicated in chorioepithelioma. From 3000 to 5000 mg.-hr. of homogenously distributed radiation throughout the uterine canal, preferably in a single application to avoid additional trauma, may be considered adequate dosage. Rigid aseptic technic with a minimum of manipulation is absolutely essential. The larger the amount of radium or radon available, the better, keeping the caliber of the applicator as small as is consistent with adequate screening. Ordinarily 100 or more milligrams for the necessary number of hours suffice. Intense irradiation with an applicator containing from 1.0 to 4.0 gm. of radium at 6, 10, or 15 cm. distance applied around the pelvis from several portals of entry probably gives the best promise of success.

Reaction. The general reaction may be marked by malaise, nausea, and vomiting during the application. General weakness, anorexia, and constipation may persist for many days in weakened or exsanguinated patients. Recovery from the reaction is accomplished by the fourth or fifth week. Local hemorrhage may follow instrumentation. Secondary infection with fever and a stormy postirradiative period may follow the application. Marked sloughing and discharge of the putrefactive, destroyed tissue follow heavy irradiation of extensive radiosensitive growths. Embolic extension may complicate the treatment, and if known beforehand to be present, irradiation should not be given. Favorable cases end in recovery if the growth was local and treatment adequate. Local recurrences may follow, and delayed secondary growths are apt to appear.

Prognosis. The prognosis is exceedingly grave. Reports of chorioepithelioma treated with radium are few. Theoretically, radium is the best method available at present for this rapidly growing, most malignant of all neoplasms.

Endocervicitis (chronic)

Diagnosis is not discussed in this outline but should be established by biopsy and by visual examination and appropriate laboratory tests in every instance. (See p. 13.)

Pathology. The lesion is a chronic inflammatory process in the endometrium, chiefly of the cervix, accompanied by hypertrophy of the endocervical glands, increase in stroma, occasional polypoid elevations, and small retention cysts of cervical glands, with a resulting chronic mucopurulent discharge. Erosions, fissures and distortion of the cervix may follow. In late stages the glandular elements may be atrophied and a single flat layer of squamous cells may line the cervix.

Radium Indications. Radium rays have frequently proved valuable as an agent to clear up a chronic leucorrhea due to longstanding inflammation in the endocervical glands. It is probable that that property of the rays which destroys to a large extent the hypertrophied glandular element in the first 3 mm. of tissue depth and which allows regeneration from the deeper portions of the glands is the curative agent in the treatment of endocervicitis. The regenerated tissues from the deeper portions of the cervical glands do not partake of the hypertrophic character of the original endometrium. The vascular changes and subsequent increased fibrosis may play a considerable part in the clearing-up of the condition. All foci of infection outside of the cervical glands must be ruled out, e. g., infection of Skene's ducts, Bartholin's gland, and such other pelvic pathology and vulvovaginal inflammation as may be found. Curettage of the corpus and cervix separately aids in establishing accurately the location of the inflammatory process.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. A dose of 350 to 700 mg.-hr. of radium evenly distributed from the external os to slightly beyond the internal os, employing the beta ray screen or a screen allowing the passage of only a small percentage of the beta rays, is the average treatment employed in carefully selected

cases of endocervicitis. The dosage may be repeated after nine or twelve months if the condition is obstinate. The effect of the radium treatment on menstrual function should subside within a year; it is perhaps best to delay the second application until the expiration of that time.

Reaction. The general reaction is usually mild when the smaller dosage is used. With 700 mg.-hr. a few days of malaise, anorexia, and nausea may accompany and follow the treatment. In patients near the menopause, 500 to 700 mg.-hr. intracervical application may cause menstrual disturbances and occasionally hasten menopause. Locally, the reaction is characterized by increased discharge, lasting several weeks or months. The endocervical reaction begins within a few days as an inflammatory swelling with disintegration of the first 2 or 3 mm. of glandular tissue. Necrosis and sloughing continue for three or four weeks, followed by gradual repair and replacement of the superficial ulceration by fine fibrous connective tissue and regenerative glandular structure from the depth of the endometrium. A decrease in the vascular supply gradually becomes manifest, due to local obliterative endarteritis. The discharge may decrease gradually or may become thin and non-irritating in character. The destruction of the endocervical hypertrophic and offending tissue is sought, in the hope that the regenerated tissue will be free from endometrial chronic inflammatory process, which is the causative element of the disease. When the latter is of bacterial or other local chronic irritative character, the results are usually excellent.

Second applications, if delayed many months, result in a similar reaction with the same local changes. If pelvic infections are present in the adnexa, vagina or urethra, they are apt to be stimulated to acute exacerbation if not eradicated before the radium treatment. Contraction of the cervix by scar tissue during or subsequent to the reaction may stenose the canal; this should be avoided by occasional cervical dilatation. Within three or four months favorable cases are freed from irritating discharge, and the general health is often greatly improved. The discharge may continue but it is apt to be of a thin, non-irritating character. A few unfavorable cases do not seem to be benefited, but

usually in such cases some other unrecognized or missed pelvic pathology may account for the failure.

PROGNOSIS. Selected cases of endocervicitis, in which all other pelvic, vaginal and urethral pathology has been eliminated, do well under radium treatment. A large proportion of the cases are clinically cured. Careful study and accurate diagnosis are required to select the cases of leucorrhea which are suitable for radium treatment.

REFERENCES

CURTIS, A. H. Chronic leukorrhea: its pathology and treatment. *J. A. M. A.*, 74: 1706, 1920.

CURTIS, A. H. Problems concerning infections of cervix, body of uterus, and fallopian tubes. *J. A. M. A.*, 80: 161, 1923.

CURTIS, A. H. The pathology and treatment of chronic leucorrhea, a further clinical and laboratory study of the subject. *Surg., Gynec. & Obst.*, 37: 657, 1923.

FLOTHOW, M. W. Chronic endocervicitis. *Nebraska M. J.*, 8: 132, 1923.

LAILEY, W. W. Endocervicitis. *Canad. Pract.*, pp. 49–52, 1924.

UTERINE FIBROMYOMA (FIBROID)

Diagnosis is not discussed in this outline, but should be established by careful examination in every instance. When doubt exists as to the correctness of the diagnosis, radium therapy should not be employed. (See p. 13.)

PATHOLOGY. Fibromyoma begins as myoma, and, as it grows, presents much connective-tissue proliferation which is believed to represent atrophic muscle fibers. These tumors may grow to enormous size and are often multiple. They may be intramural, subserous, or submucous in location. Vascular disturbances are common, with edema, and fatty or hyaline degeneration. Central necrosis, gangrene or calcification are some of the common pathological changes. Myomas may be the site of secondary infection. They are accompanied by an increased incidence of uterine carcinoma, probably due to location irritation. Excessively vascular tumors, either with normal blood vessels or abnormal blood vessels with thin walls, are often the cause of an alarming menorrhagia or metrorrhagia, or both. Large fibroids may cause symptoms by pressure on surrounding vital structures, such as the bladder, the rectum, uterine

vessels, nerves, etc. Fibroids may enlarge or remain stationary at any stage; they may degenerate by fatty, hyaline or cystic processes; they may become necrotic, gangrenous or calcified; or they may regress to a small atrophied remnant. Malignant degeneration of fibroids is not uncommon, and when they are found in association with carcinoma of the body or cervix, the question arises as to the etiologic rôle of fibroids in malignant disease of the uterus.

Radium Indications. Radium therapy has repeatedly caused regression of fibromyomata to benign stationary remnants. The property of the rays responsible for this change in fibroids may be that of a specific action on hypertrophic and hyperplastic myomatous tissue. It may be that the gamma rays have the power to transform fibrous connective tissue into finer fibrils, or it may be the action of the rays on the vascular supply, causing obliterative endarteritis of abnormal vessels rapidly and of normal vessels gradually, thus starving the neoplasm to its eventual atrophy. Another possible action may be the effect of the rays on the highly susceptible ovarian tissue. However, the great regularity with which one may produce good results with moderate intrauterine dosage casts some doubt on the rôle of ovarian changes due to radium rays. The intensity of the rays diminishes as the square of the distance. The distance from radium to ovaries varies greatly; therefore, there is a fourfold variation in the amount of irradiation received by the ovaries. The therapeutic effect of moderate dosage is almost always the same. Therefore, it may be said that the ovarian changes vary to a much greater extent than do the therapeutic results. It is probable that a certain part of the good effect from the intrauterine radium therapy is due to ovarian changes, but the evidence would indicate that these changes play a minor part. Small intramural fibroids, with excessive uterine bleeding, offer the best indications for radium treatment. Fibroids of the uterus are readily accessible for treatment and observation. Adnexal inflammatory processes, if acute or subacute, contraindicate radium therapy. Such inflammations are prone to undergo acute exacerbation as a reaction to radium treatment. Degenerative, calcified, pedunculated, submucous and subserous

fibroids and those larger than a four-months' pregnancy are unsuited for radium treatment. It is probably best not to employ radium to treat fibroids of considerable size causing symptoms during the childbearing period. If ovarian cysts of any appreciable size are present, question at once arises as to the value of radium. Tumors giving pressure symptoms should not be irradiated since the preliminary inflammatory swelling may markedly increase the pressure.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The cavity method of application, employing the gamma ray, is almost exclusively used in the treatment of fibromyomata. Heavily screened tubes are inserted into the uterine canal and lodged as close to the tumor as possible. The dosage varies from 1000 to 3000 mg.-hr. The amount of radium varies from 50 mg. up. Enlarged uteri with multiple fibroids require longer applicators with homogeneous distribution of the radium throughout the involved area and consequently a greater milligram-hour dosage than need be given to small single fibroids. The technic ordinarily employed is dilatation and curettage, almost as a routine, followed at once by the intrauterine insertion of the radium applicator with the radium arranged to deliver radiation as evenly as possible throughout the tumor. Intrauterine gauze packs are usually necessary to insure retention of the radium applicator in place. A cervical suture, with or without the uterine gauze pack, is often helpful. The bladder and rectum had better be packed away as far as possible, distance being of greater value as a screen than most of the ordinary filters interposed. The placing of radium applicators in the vault of the vagina against the lower portion of the uterus and the supplementing of this treatment by deep external irradiation over the fundus is practiced with success in cases where dilatation cannot be done. However, the amount of radium required and milligram-hour dosage must be increased many fold, according to the square of the increased distance between the radium and the tumor. The dosage varies from 700 to 3000 mg.-hr. depending upon the size of the tumors, and

their number and extent. A smaller dosage often requires subsequent treatment in four to six months. Dosages from 1200 mg-hr. up are designed for a single therapeutic application. Re-treatment with a given dosage is indicated after two months, if the tumor continues to enlarge, or at the end of six months if the shrinkage has discontinued and if troublesome symptoms persist. Excessive bleeding following irradiation rarely occurs, but may require repeated uterine packing if continuous and excessive. Re-treatment is not indicated inside of three months if the initial dose exceeded 1200 mg.-hr.

Reaction. The general reaction may be mild or marked, but it is rarely severe. Nausea, cramp-like pains in the lower abdominal region and occasional vomiting may occur during the application. Occasionally the temperature may go as high as 102° F. for a few days, but it usually subsides without serious import. Ordinarily these symptoms subside when the applicator is removed. Free elimination by the bowel and genitourinary tract is indicated during and following the treatment. Locally there may be free bleeding from the uterus for several days, although ordinarily it is not marked, and it disappears within a week. Such bleeding is more apt to be brief if the application is made shortly after menstruation. The first period after treatment may be unchanged, more excessive and prolonged, or it may be scant. The second period may be absent, scant, or normal, but rarely excessive. The third period is usually absent or scant; but if excessive, a special investigation is required to determine the cause. Patients menstruating after the third period following doses of 1200 mg.-hr., or more, may be suffering from complications within the uterus, or from some general disorder and should be under careful medical investigation. There may occur a preliminary swelling of the tumor, lasting a week or ten days, due to the immediate radium reaction. This swelling is transient and usually not marked. A gradual, progressive decrease in the size of the mass is the usual result, although it may shrink rapidly in pure myomatous, early growths. Often the process of shrinkage continues for six months or even longer. Decrease is due to shrinkage in the size of muscular and fibrous

elements of the tumor. Obliteration of the vessels reduces vascularity which may accompany or cause the general atrophy of the mass.

Regrowth of the same masses or others may occur occasionally after six months to a year, or even later. In favorable cases bleeding is stopped permanently within a few weeks. The patient makes a rapid improvement in the blood picture and in general health. At the end of six months fibromyomata disappear or decrease to a benign stationary fibrous remnant. Unfavorable cases, which are few in well-selected groups, may continue to bleed so excessively as to require uterine packing, or the tumor may react unfavorably by not decreasing in size. Fibroid tumors, carefully selected for radium treatment, and not responding by the third month after treatment, are probably complicated by other pathology unrecognized before. These possible complications include carcinoma of the body of the uterus, old sclerotic fibroids, tumors having undergone calcification, gross pathology of the adnexa, or general vascular disease, unrecognized or underestimated at the outset. Complications are few. Latent tubal or ovarian infection may be lighted up. Rapid degeneration of the tumor may result in necrosis with toxemia, with the possible development of a surgical emergency. Ovarian changes of a serious nature are rarely encountered.

Prognosis. Selected cases of fibromyomata associated with menorrhagia or metrorrhagia are permanently cured by accurately dosed treatment with radium. Patients under thirty-five years of age, with fibroids of moderate size, had better not be irradiated, since dosage sufficient to clear up the symptoms may bring on an amenorrhea, which, while lasting only six to fourteen months, may be undesirable. Patients approaching forty years of age, falling within the indicated class, are permanently cured with practically no mortality in a very high percentage of the cases. Small intramural fibroids with menorrhagia and metrorrhagia present the most favorable indication in the whole field of radium therapy.

Case History

Uterine fibroid. Prolonged uterine bleeding for two years. Loss of weight. Anemia. Uterus nodular and irregular. Twelve-hundred mg.-hr. of intrauterine application with beta ray screen, using 50 mg. of radium element for twenty-four hours. No bleeding after treatment. Clinically well five years later.

References

Abbé, R. Uterine fibroids, menorrhagia, and radium. *Med. Rec.*, 87: 379, 1915.

Beclere, A. Radiotherapy of uterine fibromyomas. *J. de radiol. et d'électrol.*, 4: 297, 1920.

Begouin, P. Hemorrhagic fibromas and radiations. *Gynec. et Obst.*, 7: 369, 1923.

Begouin, P. Incomplete abdominal hysterectomy for fibroma. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 255, 1924.

Case, J. T. Comparison of the operative and radiotherapeutic treatment of uterine myomas. *Surg. Clin.*, 1: 579, 1917.

Corscaden, J. A. Statistics and technic in the treatment of fibromyoma of the uterus by radiotherapy. *Am. J. Roentgenol.*, 9: 812, 1922.

Corscaden, J. A. The limitations of radiotherapy in the management of fibromyoma of the uterus. *Am. J. Obst. & Gynec.*, 6: 42, 1923.

Delavan, B. D. The effects of radioactivity upon nasopharyngeal fibroma. *Med. Rec.*, 87: 1056, 1915.

Essen-Moeller, E. Surgery and radium in the treatment of myomas in the women's clinic of Lund. *Rev. franc. de gynec. et d'obst.*, 16: 594, 1921.

Fabre and Gagey. The use of radium for the treatment of fibromas. *Bull. Soc. d'obst. et de gynec. de Paris*, 12: 98, 1923.

Fabre, S. Results in a series of uterine fibromas treated by radium. *Bull. Soc. d'obst. et de gynec. de Paris*, 12: 169, 1923.

Faure, J. L. Radium therapy of uterine fibromas. *Gynec. et Obst.*, 4: 290, 1921.

Gellhorn, G. When to operate and when to use radium on fibroids of the uterus. *J. A. M. A.*, 78: 259, 1922.

Gilbert, W. H. Uterine myomata and their treatment. *Calif. State J. M.*, 21: 5 1923.

Goullioud. Indications for myomectomy, hysterectomy and curietherapy in the treatment of uterine fibromas. *Rev. franc. de gynéc. et d'obstét.*, 19: 713, 1924.

Heaney, N. S. Radium versus operative treatment of fibroids. *Surg., Gynec. & Obst.*, 35: 625, 1922.

Jorgensen, P. Operations on some cases of fibromyoma unsuccessfully treated with roentgen rays. *Acta gynec. Scandinav.*, 3: 218, 1924.

Kelly, H. A. The radium treatment of fibroid tumors. *Surg., Gynec. & Obst.*, 20: 271, 1915.

Kelly, H. A. Two hundred and ten fibroid tumors treated by radium. *Surg., Gynec. & Obst.*, 27: 402, 1918.

Kohlmann, W., and Samuel, E. C. Radium therapy in fibroid and other benign conditions of the uterus. *South. M. J.*, 14: 703, 1921.

Lundquist, B. Radiotherapeutie treatment of uterine myomas at the radium institute of Stoekholm. *Acta radiol.*, 1: 524, 1922.

Miller, J. C. Radium treatment of myoma of the uterus and myopathie bleeding. *Surg., Gynec. & Obst.*, 34: 593, 1922.

Miller, J. C. Radium in the treatment of fibroids of the uterus. *Am. J. Roentgenol.*, 16: 228, 1926.

Mundell, J. J. Uterine fibroid treated with radium. *Virginia M. Monthly*, 49: 14, 1922.

Nichols, B. H. The applieation of radiation to fibroid tumors of the uterus. *Ohio State M. J.*, 21: 87, 1925.

Nogier, T. The radium treatment of uterine fibromyoma. *Arch. d'electric. med., etc.*, 30: 243; 257, 1922.

Pouey (Montevideo). Radium therapy and uterine fibromatosis. *Bull. Soc. d'obst. et de gynec. de Paris*, 12: 93, 1923.

Ransohoff, J. L. Radium treatment of uterine fibroids. *Lancet-Clinic*, 115: 116, 1916.

Roos, E. C. The treatment of fibroids of the uterus. *Illinois M. J.*, 45: 50, 1924.

Schmidt, R. Radiotherapy of myomas and hemorrhagie metropathies since 1914. *Strahlentherapie*, 13: 385, 1922.

Stenger. Pregnaney and birth after x-ray treatment of myomatous uterus. *Schweiz. med. Wchnschr.*, 51: 1084, 1921.

Taussig, F. J. In what eases do uterine fibroids still require operative removal. *J. A. M. A.*, 77: 357, 1921.

Violet, H. Surgery or radiotherapy in the treatment of uterine fibromyoma. *Rev. franc. de gynec. et d'obst.*, 19: 97, 1924.

Williams, J. D. The roentgen ray treatment of fibroids of the uterus and of menorrhagia and of metrorrhagia not due to malignaney. *Am. J. Roentgenol.*, 11: 252, 1924.

Uterine Bleeding (menopause; essential; in fibrosed uteri)

Diagnosis is not discussed in this outline but should be established by careful examination, supplemented by biopsy, to exclude other possible diagnoses. (See p. 13.)

Pathology. Excessive bleeding from the uterus, menorrhagia and metrorrhagia, may occur at any time during menstrual life. A common form is that occuring near the menopause, usually associated with a large boggy uterus, with increase in fibrous tissue without other demonstrable gross pathology. Fibrosed uteri occur in later menstrual life up to the time of the menopause. The causes are often unknown. Examination reveals no gross pathology except slight enlargement and lack of firmness in the organ. Essential, idiopathic or myopathic uterine hemorrhage

may occur in young patients. No gross pathology can be found. Chronic endometritis may cause excessive uterine bleeding. Microscopically no common pathologic findings

Fig. 23. Typical Radium Application in Uterine Bleeding. Intrauterine radium applicator containing 50 mg. held in place by deep cervical stitch and vagina packed with gauze. Dosage 1200 mg.-hr.

are in evidence in these cases. Passive congestion, marked vascular dilatation, chronic metritis may be found in the endometrial scrapings. Uterine hemorrhage due to adnexal disease or inflammation or due to general systemic disorders are not included in this group. In general, the condition included in this group may be considered as excessive uterine bleeding without demonstrable gross pathology.

Radium Indications. Radium rays, both beta and gamma, have repeatedly been demonstrated as a useful

measure to permanently cure or effectively check uterine bleeding. The properties of the effective radium rays are: (1) cell destruction of the endometrial lining with subsequent healing and fibrous tissue replacement; (2) obliterative endarteritis, decreasing the endometrial blood supply; (3) a probable effect on ovarian function, thus inhibiting excessive menstruation. The condition is of easy access for treatment and observation. The mortality is nil. Complications and sequelae are rarely serious. Uterine bleeding at the menopause is best treated by a dosage of radium causing permanent amenorrhea and precipitating the menopause. In younger women, where childbearing must not be interfered with, the dosage may be smaller than that required to bring on the menopause. Young girls may be relieved of their condition by relatively small doses without serious complications or sequelae.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The intrauterine application of a radium capsule, screened with 0.5 mm. of silver or its equivalent, allowing 10 to 15 per cent of the beta rays to act on the endometrium, may be employed with success. The milligram-hour dosage is generally lower in those applications allowing 10 to 15 per cent of the beta rays to penetrate than in those employing gamma rays only. Dilatation of the cervix sufficient for the insertion of the applicator is required. The applicator should be as long as the uterine canal, in order to afford a homogeneous distribution of the radium radiation throughout its length. A cervical stitch insures the retention of the applicator in place. Vaginal or uterine packs, or perhaps both, may be employed. The bladder and the rectum should be packed as far as possible from the radium when employing applications of 700 mg.-hr. or more. The dosage required to produce a complete amenorrhea in properly selected cases of uterine bleeding averages 1200 mg.-hr., with 600 to 800 as the minimum when 0.5 mm. of silver is used as the filter. The dosage of 1200 mg.-hr. with either the beta ray or the silver screen, well distributed along the uterine canal, suffices to produce permanent

amenorrhea in those cases of fibrosis uteri where preservation of the possibility of motherhood is not an essential feature. Young girls with essential uterine hemorrhage may safely be subjected to an intrauterine dosage of 200 to 400 mg.-hr. with beta ray screen or employing 5 per cent of the beta rays.

Treatment may be repeated in from four to six months, or a second lesser dosage may be given sooner, if the primary result was incomplete. In severe essential uterine bleeding, where hysterectomy is the only alternative, the dosage may approach 1200 mg.-hr. with a screen to exclude all but gamma rays, or 1000 mg.-hr. with a 0.5 silver screen, the risk of permanent amenorrhea being justified by the urgency of the condition. In patients under thirty years of age, with this dosage, normal menstruation is resumed in from twelve to eighteen months. Except in young girls, the tendency seems to be toward giving the therapeutic dose as indicated at one séance rather than in divided doses.

Reaction. The general reaction is usually not severe. Nausea, cramp-like pain in the lower abdomen, and sometimes vomiting comprise the symptoms of the occasional severe general reaction. The presence of a foreign body in the uterine canal may account for this reaction. Within a few weeks, symptoms of the menopause may occur, or they may become accentuated in patients already at the menopause. With light dosage, young girls seldom experience more than malaise. Locally, the bleeding usually ceases within a few days, never to reappear, following heavy dosage at or near the menopause. In many patients there may occur one, two, and occasionally three menstrual periods after the treatment, varying in character from scant to excessive. The large majority of patients menstruate scantily or not at all at the third postirradiation period and experience permanent amenorrhea thereafter. Young girls who are given doses of from 200 to 400 mg.-hr. experience reduction of menstrual flow to normal far more often than excessive or unaltered menstruation. Second doses, administered four to six months after the first, usually clear up the disorder. Radium therapy may be given more boldly in cases where hysterectomy is the only alternative. The

attempt should be made, if possible, to avoid interfering with possible childbearing, even at the risk of long convalescence or repeated dosage in young patients. Childbearing after intrauterine radium treatment is not uncommon. Spontaneous abortions are probably more numerous and it is possible that abnormal babies may result from such pregnancies, though definite proof of this eventuality is lacking. The menopause thus artificially produced is apt to be shorter than the normal, though such a statement can only be one of opinion. The artificial amenorrhea produced by radium treatment in women under thirty-five years of age may persist for many months, only to be followed by a resumption of menstruation in twelve to eighteen months. This offers more evidence that irradiation of the ovary is a minor factor in the result obtained from the radium treatment of uterine hemorrhage. The exact dosage which can be relied upon to produce permanent amenorrhea in young patients is probably not known. Dosages below 700 mg.-hr. may produce permanent amenorrhea in patients near the menopause, but it cannot be relied upon to do so. Such dosage in young women probably will not produce permanent amenorrhea but it cannot be relied upon not to do so. Recurrence of uterine hemorrhage rarely occurs in women past thirty-five years of age, after the intrauterine application of 1200 or more mg.-hr. Reappearance of menstruation in women under thirty-five years of age may occur after a dosage as high as 1200 mg.-hr. In young girls, a dosage of 200 to 400 mg.-hr. may be considered as only a controlling application, with practically no risk of permanent amenorrhea.

Prognosis. The radium treatment of uterine hemorrhage, due to undemonstrable gross pathology, is one of the most successful measures in the field of radiotherapy. In general, its use in carefully selected cases of this type of uterine hemorrhage at any time during menstruation is attended with permanent curative results in probably 95 per cent of the cases. There are few instances in the whole field of medical practice where results are secured which approach in efficiency those obtained by radium in uterine hemorrhage.

Case History

Mrs. R. Aged forty-five. Uterine bleeding. Irregular and increasing bleeding for past seven months. No demonstrable pathology. Dosage of 1200 mg.-hr. intrauterine with beta ray screen using 50 mg. radium for twenty-four hours. First postirradiation period severe. Clinically well five years later.

References

Blacker, G. The treatment of menorrhagia by radium. *Arch. Radiol. & Electroth.*, 28: 47, 1923. *Lancet*, 1: 421, 1923.

Bower, J. O., and Clark, J. H. Radium and hemorrhage. *Am. J. Roentgenol. & Rad. Therap.*, 17: 247, 1927.

Clark, J. G., and Keene, F. E. Uterine hemorrhage of benign origin treated by irradiation. *J. A. M. A.*, 79: 546, 1922.

Clark, J. G. Irradiation treatment of myopathic hemorrhage. *Surg., Gynec. & Obst.*, 40: 878, 1925.

Douay, E. Menorrhagia in young girls. *Gynec. et Obstet.*, 7: 501, 1923.

Emmett, J. M. Radium therapy in uterine hemorrhage. *Virginia M. Monthly*, 51: 562, 1924.

Emmett, J. M. An analysis of sixty uterine hemorrhage cases treated with radium. *Internat. J. Surg.*, 38: 181, 1925.

Flatau, S. The cure of climacteric hemorrhage of the uterus by radium. *Munchen. med. Wchnschr.*, 69: 1277, 1922.

Forsdike, S. Radium in the treatment of uterine hemorrhage. *Lancet*, 1: 1309, 1923. *Proc. Roy. Soc. Med. Sect. Obst. & Gynaec.*, 16; 69, 1923.

Heyman, J. Results of the radium treatment of climacteric hemorrhage at the radium institute of Stockholm. *Acta radiol.*, 1: 470, 1921–1922.

Keith, D. Y. Uterine hemorrhage in the adolescent patient treated by irradiation. *Urol. & Cutan. Rev.*, 28: 296, 1924.

Keith and Keith. Radiation in benign affections of the uterus. *Kentucky M. J.*, 22: 264, 1924.

Kelly, H. A., and Burnam, C. F. Radium in the treatment of uterine hemorrhage and fibroid tumors. *J. A. M. A.*, 63: 622, 1914.

Kennedy, W. H. Present status of radium in the treatment of uterine hemorrhage. *Indianapolis M. J.*, 28: 34, 1925.

Kupferberg, H. Radium therapy of benign uterine hemorrhage. *Fortschr. a.d. Geb. d. Roentgenstrahlen*, 29, June, 1922.

Kupferberg, H. Temporary sterilization with radium rays. *Strahlentherapie*, 22: 141, 1926.

Landham, J. W. X-ray versus radium in the treatment of uterine hemorrhage. *South M. J.*, 16: 550, 1923.

Matthews, H. B. The use of radium in the treatment of uterine bleeding other than cancer. *New York State J. Med.*, 22: 556, 1922.

Matthews, H. B. Radium in non-malignant uterine bleeding. *M. Times*, 51: 12, 1923.

Mayo, W. J. Conservation of the menstrual function. *J. A. M. A.*, 74: 1685, 1920.

Michon, et al. Very grave metrorrhagia in a young girl: persistence of the symptoms for three years in spite of many treatments with radium. *Bull. Soc. d'obst. et de gynec. de Paris*, 14: 131, 1925.

Newell, E. T. Radium in the treatment of menorrhagia and metrorrhagia. *J. Tennessee M. A.*, 15: 266, 1922.

Pemberton, F. A., Hemorrhage from the uterus in the non-pregnant woman. *Boston M. & S. J.*, 178: 485, 1918.

Polak, J. O. Notes on the clinical value of radium in the management of uterine hemorrhage. *Med. Rec.*, 101: 493, 1922.

Rhinehart, D. A. Radiation in the treatment of menorrhagia. *J. Arkansas M. Soc.*, 19: 175, 1923.

Ross, J. N. MacB., and Rolleston, H. D. Asthma and radium menopause. *Brit. M. J.*, 1: 12, 1922.

Schmidt, W. H. Radiotherapy of uterine bleeding. *Am. J. Electroth. & Radiol.*, 40: 347, 1922.

Schmitz, H., and Bundy, H. E. The treatment of benign hemorrhage of the female genito-urinary tract by radiation. *Am. J. Roentgenol.*, 10: 872, 1923.

Scott, R. A. Treatment of benign uterine hemorrhage with radium. *Illinois M. J.*, 47: 455, 1925.

Semb, O. Roentgen and radium treatment of myoma of the uterus. *Norsk. Mag. f. Laegevidensk.*, 85: 97, 1924.

Siegel, P. W. Radium castration and radium dosage. *Deutsch. med. Wchnschr.*, 49: 47, 1923.

Stacy, L. J. The treatment of menorrhagia with radium. *Minnesota Med.*, 2: 88, 1919.

Stacy, L. J. Radium treatment in 600 cases of menorrhagia. *Am. J. Roentgenol.*, 7: 379, 1920.

Stevens, J. T. The control of abnormal uterine bleeding due to benign diseases by means of radiation therapy. *Am. J. Electroth. & Radiol.*, 42: 222, 1924.

Watkins, T. J. Radium in hemorrhage at the menopause. *Surg. Clin.*, 1: 1021, 1917.

Polyps (uterine)

Diagnosis is not discussed in this outline, but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The lesion is an overgrowth of the normal elements of the uterine endometrium. Glandular structure, connective tissue, and hyperplasia of the vascular supply compose the tumor for the most part. The appearance of a polyp is usually preceded by a chronic inflammatory process in the endometrium, and it is difficult to distinguish between benign growths due to chronic irritation and true neoplastic disease. The growth may be single or multiple. If multiple, the lesions may be low and flat. Glandular hyperplasia often can not be differentiated from early malignancy. Polyps may be single and elongated, often protruding from the

external orifice. Bleeding from the uterus of the menorrhagia or metrorrhagia type is common with uterine polyps. Malignant degeneration may appear at the base or anywhere in the structure of the lesion.

Radium Indications. Radium is indicated in these lesions chiefly as a prophylactic against malignant degeneration. Irradiation of the base or site from which the uterine polyp has been removed is a distinct step forward in the control of cancer by the prevention method.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Cavity application of moderately screened radium, employing 3 per cent of the beta rays over the site of the removed polyp, is the method of choice. Dilatation sufficient to admit the applicator into the uterine cavity is required. The dosage may vary from 300 to 1000 mg.-hr., depending upon the age of the patient, the size of the site, and the relative suspicion of malignancy. If the question of possible childbearing does not enter into the management of the case, the larger doses are indicated. If the basal attachment is large or if the lesions are multiple, the heavier dosage and wider distribution are indicated. If the case history arouses suspicions of malignancy or the microscopic findings are not clearly defined, the heavier dosage is advisable. In younger women a dosage of 200 to 400 mg.-hr., accurately placed over the base of the lesion, causes no general disturbance to the patient.

Reaction. The general reaction is mild or absent with small doses. Doses of 1000 mg.-hr. intrauterine may cause malaise, nausea, cramp-like pains, and occasional vomiting with slight rise in temperature. The general reaction lasts but a few hours after the removal of the radium. Locally, a destruction of the endometrium to the depth of 1 to 3 mm. is caused by caustic necrosis produced by the hard beta and gamma rays. Fibrosis follows; endarteritis and lymphatic occlusion complete the reaction and thus prevent the development and spread of a possible malignancy. Increased discharge from the uterus results from the superficial sloughing. At the end of four to five weeks, healing is complete.

Amenorrhea may be produced and the menopause artificially induced by the larger dosage. Favorable cases return to normal as regards clinical symptoms, and do not thereafter develop carcinoma. Excessive bleeding is stopped or controlled according to the dosage of radium given. Complications are few and recurrence rarely follows adequate irradiation.

Prognosis. The basal attachment of uterine polyps that have been mechanically removed are best irradiated with radium to prevent recurrence, and as a prophylactic measure against the development of malignancy. Hemorrhage is also thereby controlled. The use of radium in this not infrequent precancerous lesion is a forward step in the prevention of cancer.

Case History

Mrs. G. Uterine polyp. Polyp protruding from os, removed by torsion. Curettement negative. Radium application of 50 mg. intracervical for ten hours employing beta ray screen. Clinically well after two years.

Carcinoma of the Uterus (cervix and corpus)

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Squamous-celled carcinoma of the cervix is the most common form of uterine carcinoma. It constitutes by far the largest number of malignancies met with in the female. It grows rapidly, invades the musculature of the uterus, spreads upward toward the body and downward to the os, involves the vaginal wall, infiltrates the parametrium, metastasizes to the regional lymph glands, and in advanced cases congeals the uterus, broad ligaments, bladder and rectum into one indurated mass. The surface is friable, ulcerated, and bleeding, and, later, a foul slough develops. Vesicovaginal and rectovaginal fistulae form when the walls of these organs slough. The lesion may be eroding and infiltrating in character, or it may be composed chiefly of proliferating cauliflower vegetations. The growth advances rapidly, and metastasizes, as a rule, early. Irregular bleeding after the menopause is oftentimes an early symptom. Early in the disease there may be indurated fissures or ulcerations, but often no visible lesion is present until the growth extends to the external os or gives warning by hemorrhage. Relatively

few carcinomata arise in the body of the uterus as compared with the cervix. On account of their location they involve other structures late. Malignant degeneration of uterine

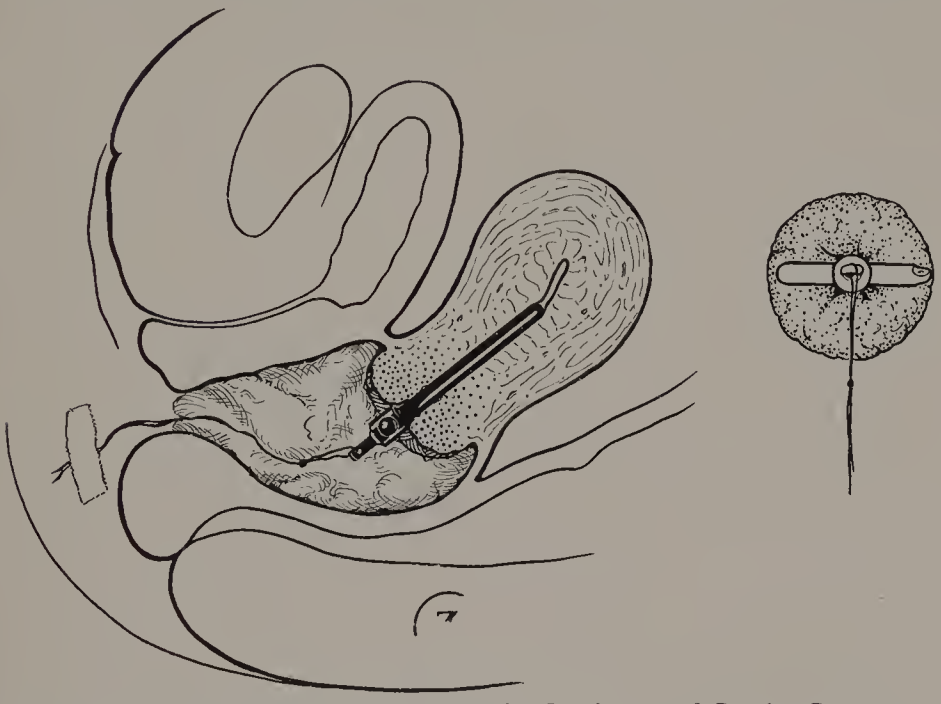


FIG. 24. Typical Radium Application in Carcinoma of Cervix. Cross arm tubal cervical applicator carrying 150 mg. of radium packed firmly in place with gauze. Dosage 3600 mg.-hr.

polyps is fairly common. The malignancy may arise at the base of the pedicle or at the tip. Adenocarcinoma arises most commonly in the body of the uterus, and rarely extends to the cervix.

RADIUM INDICATIONS. Radium therapy is indicated in all carcinomata of the cervix. It is because of the favorable results obtained in combating this lesion that much of the prominence of radium has been attained. The complete destruction of cervical carcinoma in many cases of all types and stages has brought radium to the point where it is the agent of choice in the treatment of all but the early operable cases. Even in the latter, its results alone have approximated those of surgery. In conjunction with surgery, the results obtained will in all probability excel those of either agent alone. Preoperative and postoperative irradiation of early

carcinoma of the cervix are still to be evaluated. Inoperable and advanced cases belong to the field of radium exclusively.

When palliation only is sought, radium is admittedly the agent of choice. Carcinoma of the cervix is amenable to many methods of application. The uterine walls are thick and furnish a natural screen permitting dosage not attainable elsewhere. Intrauterine and vaginal cavity application, interstitial irradiation within the lesion itself, and cross-fire from deep external irradiation, all are readily applicable with advantage to cervical carcinoma. Various complicated methods have been devised to apply radium to the pelvis. Long needles have been used to thrust radium into the broad ligament; capsules have been imbedded along the periphery of the pelvis to make a cross-fire intrauterine application and to inhibit and prevent parametrial and glandular extensions. A great variety of dosages and systematic schemes for therapy have been developed and carried out consistently over a period of years. The results in the aggregate seem to be urging the profession to the conclusion that adequate treatment of carcinoma of the cervix uteri is impossible without the aid of radium.

Malignant disease of the body of the uterus is commonly treated by hysterectomy with the possibility that radium before or after the operation tends to decrease the number of recurrences or, at least, to defer them for a longer time. Complete destruction of all malignant cells within the primary growth is accomplished, in many cases, by caustic necrosis occurring in the close vicinity of the radium, and by autolytic action at a greater distance. Those portions of the growth lying within a certain distance beyond the sphere of gamma ray necrosis undoubtedly are arrested or inhibited. Whether this inhibition is caused by direct action of the rays upon the cells, or whether the secondary fibrosis, anemia and encapsulation accomplish it, or whether the body develops an increased immunity from the destruction of the primary growth by the radium remains to be ascertained. Further advance in the treatment of malignancies must, to a large extent, depend upon this inhibition of distant growths. The cautery action of radium is responsible for most of the good result, and must be complete, thorough,

and accurate. However, the inhibitory action on distant portions of the growth must be obtained if late recurrences are to be reduced.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The most common form of radium application in carcinoma of the uterus is the intrauterine insertion of the radium capsule. The screening varies from that screen allowing the passage of from 5 to 10 per cent of the beta rays to the more commonly used beta ray screen, permitting only gamma rays to pass. The intrauterine dosage varies from 1200 or 1500 mg.-hr. to 5000 mg.-hr., the larger doses usually representing the aggregate of fractional applications. The result of experience seems to indicate giving the intrauterine dosage as rapidly as possible. The plan of a single massive dose is weighed over against fractional doses with perhaps a larger number of milligram-hours in the aggregate. Doses repeated within a few days may be considered as single applications. A preliminary mild dose, followed by a massive dose one week later, may be considered an exception, inasmuch as it is thought to give the massive dose at a time of lowered resistance in cells not destroyed by the initial but rather rendered more susceptible by it. In addition to the intrauterine irradiation, cross-fire effects are obtained by placing tubes against the cervix, in the fornices, or partially surrounding the portio vaginalis. Such applications are essential when the lesion is extensive. The beta ray screen is employed, pushing the rectum and bladder as far away from the radium as possible by means of vaginal gauze packing. Distance is of quite as much importance in the protection of the bladder and rectum as are cumbersome metal screens. It is best to keep the dosage within the vagina below 3000 mg.-hr. with the beta ray screen, except under special circumstances and with special technic.

Interstitial applications may be made directly into the lesion, employing needles of radium element or radon implants. Gold seeds of 1.0 to 2.0 mc. or various sizes of element needles should deliver from 80 to 130 mg. or mc.-hr. for each cubic centimeter of malignant tissue. Aseptic

technic is essential for the interstitial insertion of radium. Rarely an acute infection will result from the lighting-up of a latent infection already present or by the introduction of virulent organisms at the time of the insertion. When the insertion must be made through a foul field, the hazard is increased.

Where large amounts of radium are available, various mechanisms have been developed to reinforce the intrauterine irradiation. At the Memorial Hospital in New York a bomb has been constructed absorbing a large portion of the gamma rays on all but one restricted side. This beam of gamma *rays* is directed upward toward the cervix for 1000 or more milligram-hours, and to the right and left parametrial area for an equal amount. This bomb has been employed extensively in obtaining the excellent results that are secured in that clinic.

Deep external irradiation also is employed there, using a block or pack at a distance of 4 cm., with the beta ray screen, and delivering 3000 to 3200 mg.-hr. at each of six sites around the pelvis, viz., the suprapubic region, each groin, the sacrum and each sacroiliac joint—the deep external irradiation approximating 18 gm.-hr. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10, of 15 cm. distance, over each of several portals of entry, probably gives the best promise of success. Due allowance must be made for the interstitial and local irradiation. Where smaller amounts are available, 1000 mg.-hr. may be safely given to each 2 sq. in., employing a beta ray screen at 1 inch distance. The use of massive doses of deep roentgen-ray therapy has to a certain extent supplanted deep external radium treatment, probably on account of the economical aspect of the problem. On the other hand, intrauterine and intravaginal dosages between 2 and 6 gm.-hr. have been systematically given by certain clinicians over a period of years with remarkably good results. Not a few clinics, with only a moderate amount of radium available, have reported results that rival those obtained at the large radium centers.

The real field of difficulties in the treatment of uterine malignancy, as well as all carcinomatous lesions, seems to be in those portions of the growth beyond the range of the

necrosing power of the gamma rays, viz., at a distance of about 4 cm. or more. All but the very earliest cases are accompanied by a reaction of varying degree. The patients with moderately advanced carcinoma are sick. Cachectic patients tolerate irradiation poorly. If they are radiated at all, it should be only with small, fractional doses with a view to accomplishing palliation by stopping hemorrhage, drying up foul discharges and alleviating pain. When heavy irradiation is to be given in an attempt to arrest the disease permanently, general supportive measures should be instituted.

The actual intrauterine and interstitial applications should be made under aseptic technic and usually under general anesthesia. Nitrous oxide suffices in most instances, where the application is simple. A minimum of trauma is desirable. Dilatation sufficient to permit the introduction of the radium applicator into the uterus is often all that is required, and even this dilatation should be dispensed with when possible. Gauze packing or suture will hold the radium in place. Interstitial application may be made more readily if several inserters are at hand so that they may be reloaded by an assistant, thus avoiding delay between the several implantations. Mechanical or cautery removal of fungating masses may precede the radium application, but the operator faces some danger of traumatic dissemination of the growth by this precedure.

Ordinarily carcinoma of the body of the uterus is treated by intrauterine application of radium followed by hysterectomy. The dosage varies from 2 to 5 gm.-hr. with beta ray screen. The hysterectomy is done before five days or after five weeks; the latter is probably the time of choice. Extension to the ovaries is not uncommon. Recurrences may appear later in the vaginal vault, and may be treated by cavity application or by interstitial irradiation. Deep external irradiation inhibits the growth of inaccessible masses.

In carcinoma of the cervix technic widely employed in Europe gives continuous irradiation within the uterine cavity and against the cervix for five to ten days. The amount used varies from 40 to 60 mg., one half or more of which is in the interior and the remainder against the

cervix. Usually two tubes in tandem are placed within the uterus and two tubes in the vagina lying anteroposteriorly, one on each side of the cervical mass. A platinum screen, 0.5 to 2.0 mm. in thickness, or its equivalent, is used. A heavier screen is employed in the case of the vaginal radium tubes. The total dosage varies from 5000 to 10,000 mg.-hrs. The radium is removed daily, cleansed and replaced after douching the vagina. Should the temperature rise above 101.5°F., or should the leucocyte count fall below 3500, the radium is removed temporarily to be replaced when the conditions improve. Before treatment is begun all effort is made to cleanse the mass and reduce infection to a minimum, even to the extent sometimes of employing vaccines.

External irradiation is applied by using three thick lead cylinders, or "cannons," each containing 100 mg. of radium, placed over the anterior wall of the lower abdomen, centered over the cervical mass, and left in place twenty days at 10 cm. distance. The three sites are the midline and just inside the brim of the true pelvis on each side. The total dosage in some instances amounts to 140,000 mg.-hr. This external method is employed in advanced cases where the broad ligaments are involved.

Reaction. The reaction from adequate radium treatment of uterine carcinoma is usually severe. Nausea, vomiting, uterine cramps, and elevation of temperature and pulse rate may be evident while the radium is in place. As a rule, these symptoms subside when the radium is removed; but not infrequently nausea, elevated temperature, weakness, anorexia, and marked constipation may be prominent for several days. Free ingestion of fluids, hydragogue cathartics, and sodium bicarbonate seem to alleviate the symptoms. Sometimes diarrhea is a troublesome symptom. Pain may be troublesome, but seldom requires more than simple analgesics for relief. Morphine is rarely necessary, but it should be used if the general welfare of the patient requires it. Anorexia frequently interferes with the adequate nourishment of the patient. Valiant attempts should be made to nourish the patient sufficiently to prevent loss of weight, weakness and consequent lowered general resistance. Elimination must be promoted vigorously so that the toxic

material absorbed from the disintegrating local lesion may be speedily moved, and the general well-being be maintained as much as possible during the following weeks of the reaction.

Blood transfusion is a valuable aid to the patient. The blood picture should be carefully checked before and during the treatment and during the reaction period so that transfusion may be promptly done when a low hemoglobin reading appears. Rapidly falling hemoglobin figures during the treatment indicate the necessity of stopping the irradiation or of giving a blood transfusion. When the leucocyte count falls below 3500, irradiation is contraindicated; and when it reaches a point below 3000 there is danger of death. Such patients either do not survive the reaction at all or they recover very slowly. The second week sees the patient slightly improved, but, as the third week comes on, the general effect secondary to the local reaction becomes apparent. Slough from the local cauterizing effect of the radium reaches its height during the third week and toxic absorption is most marked.

Great variation in the reaction of individual patients exists. Depression with extreme weakness and all that go with them are present in some, while in others there are few symptoms except those referable to the local changes, such as pelvic pain, rectal and bladder distress.

During the fourth and fifth weeks the symptoms abate so that by the sixth week the patient should have fairly well recovered from the treatment. If the convalescence is unduly slow, it indicates inability of the patient to withstand the heavy irradiation given.

To obtain the best results, the patient must be able to recover vigorously from the treatment. This recovery depends upon a careful estimation of the patient's general condition and the adaptation of the dosage and technic to the best interests of the individual patient and lesion. It must be remembered that the radiologist is treating a patient suffering from a malignant lesion and that he is not primarily treating a malignant lesion in a patient. It is of vastly more importance to treat the patient than to treat the lesion. This statement is made advisedly and with the realization of its diverse

ramifications and its bearing upon the progress of the fight against malignancy.

Locally the clinical reaction begins from the seventh to the fourteenth day. It consists of cautery or autolytic necrosis of malignant cells within range of the radium rays. Cellular swelling, vacuolization, nuclear degeneration, and liquefaction are well advanced by the sixth or eighth day. Those cells not succumbing are in their most weakened condition at this time, hence the second and massive dose is given by some competent radiologists on about the sixth to the eighth day. Clinical changes are evident during the third week in the form of inflammatory reaction and slough. Swelling, inflammation, and slough are most evident during the third week and in most instances the patient experiences local pain. If the bladder and rectum have been too heavily irradiated, symptoms of irritation referable to these organs appear. Pain and tenesmus may be marked. Frequent and painful urination is present. Rectal tenesmus and painful defecation increase the constipation which is often marked in these cases. Increased fluid intake, urinary antiseptics, and sedatives are beneficial. Rectal suppositories of opium may be required to allay the pain. Bladder irrigation, even under local anesthesia, may have to be instituted in severe cases. Such reactions are avoidable when the dosage is properly adjusted and the bladder and rectum are sufficiently packed away from the radium. When the urgency of the treatment requires disregard of the bladder and rectal reaction these complications must be faced and managed.

Frequent mild cleansing douches serve to keep the vagina and ulcerated surfaces relatively clean, prevent the accumulation of foul, irritating discharges, and discourage adhesive vaginitis. Complete rest in bed is advised for serious lesions of the advanced types and only a little exercise should be permitted for the early cases. This program is indicated during the period of the reaction. Nourishing full diets aided by iron and bitter tonics are needed. In weakened and anemic cases, blood transfusion aids greatly in assisting the patient to endure the later reaction. Transfusion may be done as a preliminary to the treatment, or it may be repeated during the period of the reaction when indicated. General efficient

and systematic medical management before and during the treatment and the period of the reaction are fully as essential as in connection with any major medical or surgical ailment. The patient is gravely ill and should be treated accordingly.

By the fifth week reparative processes are well under way. Healing and fibrous contraction are evident. The extent of the destruction of the growth can be determined and a fair opinion may be formed as to the probable further course of the disease. Undestroyed portions of the lesion may be re-treated. Fistulae may appear if the malignancy involves the bladder or rectal wall or if their walls have inadvertently been destroyed by trauma.

With satisfactory local treatment of carcinoma, the cervix presents a shrunken, scarred, pale telangiectatic surface which gives a firm rubbery feel rather than an indurated hardness. The vaginal walls show the effects of irradiation in scarring, contractions, and vascular injection. During the subsequent months the fibrous contraction further puckers the cervix and vagina. In satisfactory reactions the uterus is movable and no indurated masses or glands can be found. If more distant secondary growths are present, they may remain quiescent for months and their enlargement only will reveal them to systematic subsequent clinical examination. Local recurrences appear, as a rule, within six months. They may appear as friable and bleeding hypertrophied masses, or they may present indurated tumors below the surface, burrowing along the path of least resistance. Late slough *en masse* of a portion of the cervix or vagina may occur several months after treatment from endarteritis and local anemia. A gray sloughing ulcerated surface is left which heals with difficulty.

Prognosis. The prognosis is grave in uterine malignancy. The results obtained in early operable cervical lesions are about on a par with the surgical results, except that there is no primary mortality in the use of radium. In all other types of cervical carcinoma radium is generally conceded to be superior to other methods of treatment. Statistics are numerous and reliable reports are many, describing the results obtained with all manner of methods and combinations of methods of treating uterine malignancies.

Crystallization of opinion has not yet been accomplished, but the trend seems to be toward the use of radium as by far the most valuable agent available in the treatment of carcinoma of the cervix. The immediate prognosis is good in any but the most advanced cases. Local clinical eradication is common. The dosage varies between 2 and 5 gm.-hr. as a minimum and between 20 and 25 gm.-hr. as a maximum. Even in hopelessly advanced cases the results are sometimes astonishing; occasionally a patient makes a clinical recovery which gives from one to three years of comparative comfort. In advanced cases palliation is all that can be hoped for. This palliation consists of the drying-up of the local lesion, the relief of pain and discharge, and the prolongation of life with eventual demise from toxemia rather than from the mutilating local destruction and filth.

Marked cachexia is a contraindication to radium treatment. However, it must be stated that it is the exceptional case in which the judicious use of radium increases suffering or shortens life.

Case History

Mrs. M. Aged twenty-nine. Carcinoma of cervix (microscopic confirmation). Bleeding, foul, ulcerated, friable mass at site of cervix uteri. Dose of 50 mg. radium element in cervical canal, with beta ray screen, for forty-eight hours, 75 mg. in mass in form of needles (13 per cent beta rays) for eighteen hours, or a total of 1350 mg.-hr. Total dosage 3750 mg.-hr. Four months later some ulceration was still present. Clinically well after four years.

References

Anspach, B. M. The treatment of advanced carcinoma of the cervix with radium. *Am. J. Obst. & Gynec.*, 72: 97, 1915.

Amreich, I. Combined radiotherapy of carcinoma of the uterus. *Zentralbl. f. Gynäk.*, 45: 1177, 1921.

Bachem, A. The physical foundations of irradiation of the uterus and the combined roentgen and radium therapy. *Strahlentherapie*, 12: 979, 1921.

Baily, H., and Bagg, H. J. Vulvar and vaginal cancer treated by filtered and unfiltered radium emanation. *Am. J. Obst. & Gynec.*, 2: 587, 1921.

Bailey, H. Radium as a prophylactic and curative agent in recurrent carcinoma of the uterus. *New York State J. Med.*, 24: 985, 1924.

Bailey, H., and Healy, W. P. Follow-up results of 908 cases of uterine cancer treated by radium. *Am. J. Obst. & Gynec.*, 6: 402, 1923.

Baisch, K. The results of radium treatment of carcinoma of the uterus. *Strahlentherapie*, 10: 36, 1920.

Barcat, J. Radiumtherapy in uterine cancer. *Progrès. méd.*, 36: 290, 1921.

Barrow, W. Treatment of malignant uterine conditions with radium. *Kentucky M. J.*, 19: 770, 1921.

Begouin. Statistics of clinical cures of carcinoma of the cervix by radium. *Bull. et mém. Soc. nat. de Chir. de Paris*, 50: 140, 1924.

Beuttner, O. The results obtained with radium treatment in carcinoma of the cervix uteri. *Schweiz. med. Wchnschr.*, 53: 105, 1923.

Boggs, R. H. Carcinoma of the uterus treated by a combination of radium and roentgen rays. *Am. J. Roentgenol.*, 4: 207, 1917.

Bonnal, G. Indications and technic of radium therapy in certain forms of carcinoma, and particularly in carcinoma of the uterus. *Marseille-méd.*, 59: 250, 404, 1922.

Bottaro, L. P., and M. Becerro de Bengoa. Radium therapy during pregnancy. *An. de Fac. de med., Montevideo*, 5: 209, 1920.

Bowing, H. H. The application of radium in operable or borderline cases of carcinoma of the cervix uteri before operation. *Radiology*, 1: 199, 1923.

Bowing, H. H. Surgery, radium and roentgen rays in the treatment of carcinoma of the cervix. *Am. J. Obst. & Gynec.*, 11: 400, 1926.

Brooks, C. D., and Clinton, W. R. Radium treatment in cancer of the cervix. *J. Michigan M. Soc.*, 22: 80, 1923.

Brooks, C. D. Radiotherapy in inoperable carcinoma of the cervix. *Am. J. Roentgenol.*, 14: 541, 1925.

Bretschneider, R. Further results of radiotherapy in carcinomas of the female genitals. *Monatschr. f. Geburtsh. u. Gynäk.*, 67: 15, 1924.

Bumm, E. Paravaginal radiotherapy. *Arch. f. Gynäk.*, 117: 221, 1922.

Burnam, C. F. Results of treatment of carcinoma of the cervix. *Am. J. Roentgenol.*, 9: 765, 1922.

Burnam, C. F., and Neill, W. A brief review of the indications and technical procedures employed by the authors in treatment of cancers of the uterine cervix and body. *Radiology*, 5: 1, 1925.

Burrows, A. The radium treatment of cancer of the cervix of the uterus. *Am. J. Surg.*, 29: 296, 1915.

Cabanes, M. A case of propagation of uterine cancer after radium therapy. *Bull. Soc. d'obst. et de gynec. de Paris.* 13: 508, 1924.

Cannon, D. The application of radium to gynecology as practiced by the Vienna school. *Irish M. J. Sc.*, 13: 20, 1923.

Cathala and Merat. Carcinoma of the cervix in pregnant women and radium therapy. *Bull. Soc. d'obst. et de gynec. de Paris*, 12: 109, 1923.

Clark, J. G. What do the newer methods of treatment offer the patient with malignant disease of the uterus? *N. York M. J.*, 102: 485, 1915.

Clark, J. G. Results obtained by the use of radium in the treatment of cancer of the uterus. *Ann. Surg.*, 64: 602, 1916.

Clark, J. G., and Keene, F. E. Treatment of cancer of the pelvic organs with moderate irradiation. *Am. J. Roentgenol.*, 9: 808, 1922.

Clark, J. G. The therapeutic value of radium in the treatment of malignant lesions of the pelvic organs. *Therap. Gaz.*, 39: 166, 1923.

Clark, J. G., and Block, F. B. Relative values of irradiation and radical hysterectomy for cancer of the cervix. *Am. J. Obst. & Gynec.*, 7: 543, 1924. *Atlantic M. J.* 27: 696, 1924.

Coffey, R. C. The relative fields of radium, surgery, and cautery in the treatment of cancer of the cervix. *Northwest Med.*, 20: 173, 1921.

Cole, P. P. The treatment of inoperable cancer of the female pelvic organs. *Brit. M. J.*, 2: 827, 1925.

Coliez, R. The physical basis in treatment of cancer of the cervix uteri by combined radium and x-ray therapy. *J. de radiol. et d'électrol.*, 7: 201, 1923.

Coulomb and Jean. Intestinal obstruction after radium treatment of carcinoma of the cervix. *Bull. et mém. Soc. de chir. de Paris*, 48: 1275, 1922

Chile, G. W. Surgery versus x-ray and radium therapy in the treatment of tumors of the uterus. *Illinois M. J.*, 45: 177, 1924.

Crossen, H. S. The choice between radium, x-ray, and the knife in the treatment of uterine myoma and uterine cancer. *J. Missouri M. A.*, 19: 55, 1922.

Daels, F. Histologic pictures representing the cure of uterine basocellular epithelioma. *Arch. Radiol. & Electroth.*, 28: 1, 1923.

Daels, F. and de Backer, P. New techniques of "Curic" therapy of cancer of cervix uteri. *Brit. J. Radiol.*, 29: 315, 1924.

Daels, F., and de Backer, P. The present status of treatment of cancer of the cervix uteri. *Nederl. Tijdschr. v. Geneesk.*, 69: 229, 1925.

Daels, F. and de Backer, P. Contribution to the technique of intra-peritoneal irradiation of cancer of the cervix uteri. *Brit. J. Radiol.*, 30: 472, 1925.

Dannreuther, W. T. Combined radium therapy and operation in the treatment of cancer of the uterus. *Am. J. Obst. & Gynec.*, 9: 608, 1925.

Debiasi, E. Factors which affect prognosis in the radio-therapy of cancer of the uterus. *Radiol. med.*, 13: 719, 1926.

Degrais, P., and Bellot, A. Cancer of the uterus and radium, clinical and histological considerations. *Canad. Pract. & Rev.*, 39: 334, 1914. *Clinique*, 9: 228; 294, 1914.

Degrais, P. Cancer of the cervix. *Arch. mens. d'obst. et de gynéc.*, 8: 623, 1919.

Delfourd, et al. Cancer of the cervix treated by radium and hysterectomy. *Bull. Soc. d'obst. et de gynéc. de Paris*, 11: 503, 1922.

Donaldson, C. O., and Knappenberger, G. E. Radium in the uterine cancer. *South. M. J.*, 15: 224, 1922.

Donaldson, M., and Canti, R. G. Fifty cases of carcinoma of the cervix treated with radium. *Brit. M. J.*, 2: 12, 1923.

Donaldson, M. Report on eighty-five inoperable cases of carcinoma of the cervix treated with radium at St. Bartholomew's hospital. *Brit. J. Radiol.*, 30: 477, 1925.

Donaldson, M. Treatment of inoperable carcinoma of the cervix uteri with radium. *Brit. M. J.*, 876, 1925.

Douay, E. Radium and carcinoma of the cervix treated. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 85, 1924.

Douay, E. The respective indications of surgery and radium and of their association of carcinoma of the cervix. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 341, 1924.

Duncan, R. The treatment of uterine cancer. *Texas State J. Med.*, 18: 366, 1922.

DUPONT. The technic of insertion of radium needles in the parametrium through the abdominal path. *Progrès. méd.*, 37: 25, 1922.

FARMER, T. Review of four years' work with radium in gynecology. *New York State J. Med.*, 25: 195, 1925.

FARRAR, L. D. P. Preliminary report of primary carcinoma of the cervix treated with radium in the women's hospital in the state of New York. *Am. J. Obst. & Gynec.*, 10: 205, 1925. *New York State J. Med.* 25: 855, 1925.

FIELD, C. E. Carcinoma of the uterus with pregnancy intervening treated successfully by radium followed by delivery of a normal child. *Am. J. Roentgenol.*, 9: 657, 1922.

FINDLEY, P. Radium treatment of cancer of the cervix. *Am. J. Surg.*, 30: 337, 1916.

FRANK, R. T. The palliative treatment of inoperable carcinoma of the cervix by means of radium. *J. Cancer Research*, 2: 85, 1917.

FRANK, L. The treatment of cancer of the uterus with radium. *South. M. J.*, 15: 489, 1922.

FRIEDLAENDER, B. Cancer of the uterus. *Internat. J. Surg.*, 35: 52, 1922.

GAGEY, J. The treatment of cancer of the uterine cervix by radium therapy. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 22–28, 1924.

GANN, D. Healing of the vesico-uterine fistula after radium. *Urol. & Cutan. Rev.*, 26: 343, 1922.

GOUVERNEUR, R., and FABRE, S. Lesions of the bladder in cancer of the uterus before and after radium therapy. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 782, 1924.

GOUVERNEUR, R., and FABRE, S. The cystoscope in cancer of the cervix of the uterus before and after curietherapy. *Gynec. & Obst.*, 11: 189, 1925.

GRAVES, W. P. Contraindications to the use of radium in gynecology. *Am. J. Obst. & Gynec.*, 9: 445, 1925.

GRAVES, W. P. Cancer of the cervix uteri. *Boston M. & S. J.*, 188: 1006, 1923.

GREENOUGH, R. B. The treatment of malignant diseases with radium and x-ray: cancer of the cervix. *Surg., Gynec. & Obst.*, 39: 18, 1924.

HALL, O. D. The use of radium in the treatment of cancer of the cervix. *J. M. A. Georgia*, 12: 45, 1923.

HARTMANN, H. Radium therapy in cancer of the cervix and corpus uteri. *Gynec. et Obst.*, 4: 301, 1921.

HEALY, W. P. Evaluation of treatment of carcinoma of the cervix with radium. *Am. J. Roentgenol.*, 14: 542, 1925.

HERTZLER, A. E. X-ray and radium in conservative gynecology. *Am. J. Obst. & Gynec.*, 4: 293, 1922.

HEUSER, C. Radium therapy of the prostate, rectum, cervix uteri, vagina, and urethra. *Semana méd.*, 29: 318, 1922.

HEYMAN, J. Final results in radium treatment of carcinoma of the cervix uteri at Radium-hemmet, Stockholm, Sweden. *Surg., Gynec. & Obst.*, 40: 161, 1925. *Am. J. Roentgenol.*, 13: 158, 1925.

HEYMAN, J. Experience and results in the radiological treatment of carcinoma of the ovary. *Acta Gynec. Scandinav.*, 3: 109, 1924.

HEYMAN, J. Technique and results of the treatment of cervix carcinoma in Radium-hemmet, Stockholm. *Strahlentherapie*, 20: 34, 1925.

Hubbard, J. E. Radium in inoperable carcinoma of the uterus. *W. Virginia M. J.*, 17: 473, 1923.

Jacherl. The behavior of protective ferments against carcinoma in operated and nonoperated cases of carcinoma of the uterus treated by roentgen or radium irradiation. *Arch. f. Gynäk.*, 119: 440, 1923.

Janeway, H. H. The treatment of uterine cancer by radium. *Surg., Gynec. & Obst.* 29: 242–245, 1919.

Jayle, F. Radiotherapy in gynecology .*Rev. franc. de gynec. et d'obst.*, 17: 561, 1922.

Jones, H. O. Report of cases treated with radium in the gyn. service at St. Luke's Hosp. *Surg., Gynec. & Obst.*, 33: 409–412, 1921.

Jones, T. E. The rôle of radium in the treatment of carcinoma of the uterus. *Am. J. Obst. & Gynec.*, 7: 541–542, 1924.

Jones, T. The rôle of radium in the treatment of cancer of the cervix. *Am. J. Obst. & Gynec.*, 9: 662, 1925.

Kaplan, I. I. A new type of applicator for use in the treatment of malignancy of the cervix. *Am. J. Roentgenol.*, 17: 360, 1927.

Keene, F. E. Radiotherapy in gynecology. *Penn. M. J.*, 20: 469, 1917.

Kehrer, E. Radium therapy. *Arch. f. Gynäk.* 117: 261, 1922.

Kelly, H. A. The treatment of cancer by radium. *Maryland M. J.*, 58: 161, 1915.

Kennedy, W. H. Superiority of radium over surgery in cancer of the uterus. *Med. J. & Rec.*, (*supp.*) 120: 148, 1924.

Klemperer, P. Histopathologic changes in uterine carcinoma treated with radium. *Am. J. Obst. & Gynec.*, 9: 619, 1925.

Knox, R. The treatment of gynecologic conditions by x-rays and radium. *Brit. M. J.*, 2: 678, 1922.

Lacassagne, A. Soft rays and hard rays in curiethcrapy of uterine cancer. *Presse méd.*, 30: 323, 1922.

Lachapele, A. The importance of mitosis in the immediate prognosis of cancer of the cervix uteri. *Arch. d'électric. méd.* 3, 31: 340, 1923.

Laffont. Vaginal hysterectomy after the application of radium. *Bull. Soc. d'obst. et de gynec. de Paris*, 14: 232, 1925.

Lahm, W. The importance of microscopic examination for the treatment and prognosis of cervical carcinoma. *Arch. f. Gynäk.*, 117: 264, 1922.

Lamarque, P., and Lachapele, A. Cure of cancer of the cervix uteri by combined radium and roentgen therapy. *Arch. d'électric. méd. Bordeaux.*, 33: 136, 1923.

LaPointe, A. Cancer of the uterus treated by radium. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 591–592, 1924.

Leclerc, C. The association of surgery and radium in cancer and particularly in cancer of the uterus. *Bull. et mém. Soc. d. Chir. de Paris*, 48: 666, 1922. *Presse méd.*, 30: 731, 1922.

Lee, J. M. Radium in surgery and gynecology. *J. Am. Inst. Homoeop.*, 9: 599, 1916.

Lenz, M. Radiotherapy of cancer of the cervix at the radium institute, Paris, France. *Am. J. Roentgenol.*, 17: 335, 1927.

LETULLE, M. The action of radium on a cancerous uterus. *Presse méd.*, 30: 121, 1922.

MALLET, L. Treatment of carcinoma of the cervix. *Presse méd.*, 31: 289, 1923.

MARTIN, A. Radiotherapy in cancer of the uterus. *Jahreskurse f. Arztl. Fortbild.*, July, 1915.

MARTIN, C. L., and ROGERS, F. T. Effect of irradiation on urcter. *Am. J. Roentgenol.*, 16: 215, 1926.

MASSAZZA, M. Histologic observations of epitheliomas of the uterus treated by radium. *Ann. di ostet. e ginec.*, 44: 671, 1922.

MAXWELL, A. F. Results of radium in gynecology. *California State J. Med.*, 21: 155, 1923.

MAYER, A. Expericnce with radiation for cervical cancer and subsequent operation. *Zentralbl. f. Gynäk.*, 46: 1599, 1922.

MILLER, C. J. Radium in thc treatment of carcinoma of the cervix uteri. *Surg., Gynec. & Obst.*, 22: 437, 1916.

MONOD, R., and MONOD, O. Treatment of carcinoma of the cervix by hysterectomy following radium therapy. *Presse méd.*, 30: 113, 1922.

MUHLMANN, E. Results of radiotherapy of cancer of the uterus. *Strahlentherapie*, 16: 137, 1923.

MUIR, J. Treatment of cervical cancer by radium emanation. *J. Maine M. Assoc.*, 17: 151, 1926.

NAUJOKS, H. Radiotherapy of malignant neoplasm in gynecology. *Deutch. med. Wchnschr.*, 50: 396, 1924.

NEEF, F. E. The treatment of advanced cancer of the cervix by vaginal and transperitoneal implantation of glass radium emanations capillaries. *Arch. Clin. Cancer Research*, 1: 67, 1925.

NEELY, S. D. Inoperable carcinoma of the cervix; report of 3 cases in which radio-therapy arrested disease. *J. Oklahoma State M. A.* 16: 113, 1923.

NORRIS, C. C. Carcinoma of the body of the uterus. *Am. J. Obst. & Gynec.*, 7: 550, 1924.

ODESCALCHI, I. Notes on 100 cases of epithelioma of the portio-vaginalis of the cervix treated by radium. *Ann. di ostet. e ginec.*, 46: 187, 1924.

OSTROIL, A. The treatment of carcinoma of the uterus with radium and radium emanations. *Prakticky Lek. Prague*, 3: 251, 1923.

PARACHE. The treatment of uterine cancer with radium. *Siglo med.*, 75: 4, 1925.

PFAHLER, G. E. A new radium applicator for the treatment of uterine carcinoma. *Am. J. Roentgenol.*, 15: 365, 1926.

PIRRI, A. Two cases of uterine carcinoma treated with radium. *Morgagni*, 63: 293, 1921.

PORTMANN, U. V. The general role of x-rays in the treatment of benign and malignant tumors of the uterus. *Illinois M. J.*, 45: 197, 1924.

PORTMANN, U. V. Radiation therapy of cancer of the uterus. *Am. J. Obst. & Gynec.*, 7: 536, 1924.

PORTMANN, U. V. Radiation therapy of carcinoma of the uterus. *Am. J. Obst. & Gynec.*, 9: 658, 1925.

POZZI, S., and ROUHIER, G. Vaginal hysterectomy supplemented by radium therapy for cancer of the uterus. *Rev. de Gynec. et de chir. abd.*, 23: 209, 1915.

Proust, R., and Mallet, L. Respective indications of hysterectomy, radium and penetrating roentgenotherapy in cancer of the cervix. *Presse méd.*, 30: 89, 1922.

Quigley, D. T. Etiology, pathology, and treatment of cancer of the cervix. *Radiology*, 5: 9, 1925.

Ransohoff, J. L. Late results of the radium treatment of cancer of the uterus. *J. A. M. A.*, 74: 163, 1920.

Ransohoff, J., and Ransohoff, J. L. Radium treatment of uterine cancers. *Ann. Surg.*, 64: 298, 1916.

Recaséns, Y. Gurol, S. (Madrid). Radium treatment of cancer of the cervix. *Arch. mens. d'obst. et de gynec.*, 8: 676, 1919.

Regaud, C., et al. Curietherapy in cancer of the cervix uteri. *J. de radiol. et d'électrol.*, 7: 510, 1923.

Richard. Radium treatment of cancer of uterine cervix. *Paris méd.* 12: 511, 1922.

Risley, E. H., and Leland, G. A. Jr. Report of treatment of carcinoma of cervix at the Huntington hospital for period of four years. *Boston M. & S. J.*, 177: 891, 1917.

Ross, J. W. Cancer of the uterine cervix. *Canad. M. A. J.*, 12: 772, 1922.

Roussy, G., and Leroux, R. The action of radium in the treatment of cancer of the cervix uteri. *Rev. de chir.*, 60: 499, 1922.

Schmitz, H. Radium and mesothorium in uterine cancer. *Internat. Abstract. Surg.* 20: 8, 1915.

Schmitz, H. The treatment of cancer of the uterus. *J. A. M. A.*, 77: 608, 1921.

Schmitz, H. Technic and statistics in the treatment of carcinoma of the uterus and contiguous organs with the combined use of radium and x-rays. *Am. J. Roentgenol.*, 60: 499, 1922.

Schmitz, H. The technic of the treatment of carcinoma of the cervix uteri with a combination of x-rays and radium rays. *Am. J. Roentgenol.*, 10: 219, 1923.

Schmitz, H. Histologic and clinical studies of cervical carcinomas treated with gamma and x-rays. *Northwest. Med.*, 22: 232, 1923.

Schmitz, H. The clinical significance of chemical and serum analyses of the blood of uterine cancer carriers subjected to measured radiation doses. *Am. J. Obst. & Gynec.*, 7: 449, 1924.

Schmitz, H. Five year end-results obtained in carcinoma of the female pelvic organs, with special reference to radium x-ray therapy. *Surg., Gynec. & Obst.* 39: 775–780, 1924.

Schmitz, H. End-results of the treatment of cervical carcinoma with radium and roentgen rays. *J. A. M. A.*, 84: 81, 1925.

Schmitz, H. The treatment of inoperable cervical carcinomata with measured doses of x-rays and radium based on microscopic examinations. *Am. J. Obst. & Gynec.*, 9: 644, 1925.

Schmitz, H., et al. The significance of the histological "malignancy index" for prognosis and treatment of carcinomas of the cervix uteri. *Am. J. Roentgenol.*, 16: 30, 1926.

Scholten, G. C. J. Results of radiotherapy of carcinoma of the uterus. *Münch. med. Wchnschr.*, 70: 300, 1923.

SCHREINER, B. F., and KRESS, L. C. Clinical results after irradiation of cancer of the cervix uteri. *New York State J. Med.*, 24: 981, 1924.

SCHREINER, B. F. A report of sixteen cases of adenocarcinoma of the cervical canal treated by radium and x-rays. *Arch. Clin. Cancer Research*, 1: 31, 1925.

SCHREINER, B. F. SIMPSON, B. T. A summary of the results in the treatment of adenocarcinoma of the fundus of the uterus by radiation. *Arch. Clin. Cancer Research*, 1: 35, 1925.

SEITZ, L. Five years' experience with radiotherapy of carcinoma of the uterus. *Arch. f. Gynäk.*, 117: 258, 1922.

SELLERS, T. B. The use of radium in the treatment of benign and malignant conditions of the uterus. *New Orleans M. & S. J.*, 77: 217, 1924.

SFAMENI, P., and MASOTTI, A. New radio-active devices for gynecologic therapy. *Clin. ostet.*, 24: 86, 1922.

SHROYER, F. I. Uses of radium in malignant and nonmalignant conditions with particular reference to the field of gynecology. *Ohio State M. J.*, 19: 498, 1923.

SKEEL, R. E. Some phases in the evolution of the diagnosis and treatment of cancer of the cervix. *Am. J. Obst. & Gynec.*, 3: 252, 1922.

SMITH, W. S. Gynecological conditions treated with radium alone or combined with surgery. *Surg., Gynec. & Obst.*, 40: 598, 1925.

STACY, L. Treatment of carcinoma of the body of the uterus. *Radiology*, 5: 331, 1925.

STONE, W. S. The present position of radium in the study and treatment of uterine cancer. *Surg., Gynec. & Obst.*, 32: 509, 1921.

STRACHAN, G. I. Radium treatment of inoperable carcinoma of the cervix. *Brit. M. J.*, 1: 879, 1925.

TAUSSIG, F. J. Irradiation in cancer of the cervix. *Radiology*, 5: 5, 1925.

TATE, W. Radium treatment of carcinoma uteri. XIII Internat. Cong. Med., London.

TYLER, A. F. Radiation treatment of uterine cancer. *Nebraska M. J.*, 7: 162, 1922.

WARD, G. E. Radium in treatment of cancer of cervix uteri. *J. A. M. A.*, 87: 1697, 1926.

WARD and FARRAR. Radium treatment of carcinoma of the uterus. *Am. J. Obst. & Gynec.*, 11: 439, 1926.

WERTHEIMER, S. Metastases from irradiated and non-irradiated carcinomata of the cervix. *Strahlentherapie*, 12: 90, 1921.

WESTMAN, A. The results of prophylatic postoperative radiologic treatment of carcinoma of the uterine cervix at radiumhemmet in Stockholm. *Acta Radiol.*, 3: 502, 1924.

WILLIS, G. S. Radium treatment of fibroid tumors of uterus. *Med. J. & Rec.*, (supp.) 120: 146, 1924.

WILSON, R. T. Roentgen ray treatment of carcinoma of the uterus. *Texas State J. Med.*, 20: 431, 1924.

WINTER, R. Experience with radiotherapy of inoperable carcinoma of the cervix of the uterus. *Strahlentherapie*, 15: 473, 1923.

WOODALL, C. W. Radium as a substitute for hysterectomy. *Am. J. Obst. & Gynec.*, 6: 734, 1923.

ZBINDEN, T. The action of radium upon cancer of the cervix. *Ohio State M. J.*, 20: 14, 1924.

ZWEIFEL, E. The importance of radiotherapy in the treatment of carcinoma of the cervix. *Strahlentherapie*, 14: 605, 1922.

ZWEIFEL, E. Radiotherapy for carcinoma of the cervix uteri. *Strahlentherapie*. 15: 118, 1923.

CARCINOMA OF THE URETHRA, VULVA AND VAGINA

Diagnosis is not discussed in this outline, but should be established by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. Primary carcinoma of the urethra, vulva or vagina is rare. The growth is squamous-celled in type. Probably the most common site of all is in the labia minora where the growth may arise on the basis of an old leucoplakia. The urethra may be the seat of carcinoma in the female, though it rarely occurs there in the male. Surface proliferation with ulceration, and rapid local extension are the rule, with the lesion more apt to be excavating than hypertrophic or vegetative in character. Metastases occur early to the inguinal glands. Primary urethral carcinoma is rare but it does occur. Secondary growths in the vagina, urethra and vulva are not uncommon from lesions in the uterus, rectum or bladder.

RADIUM INDICATIONS. Radium is the agent of choice in dealing with malignancies in these structures in all except the earliest cases. The lesions are unusually accessible for treatment and observation. Malignant cells here, as elsewhere are amenable to the necrotic action of both beta and gamma rays. Both the caustic and the autolytic action can readily be employed, aided by cross-fire by gamma irradiation from the vagina, rectum and by external applications. Favorable results can be obtained with a minimum of tissue destruction. Gold implants or radium element needles may be used for interstitial application, while capsules are better suited for surface or cavity irradiation. Deep external irradiation may be used to advantage, especially in vulvar and urethral tumors.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. In vulvar carcinoma interstitial application with gold implants of 1.0 to 2.0 mc. each per cubic centimeter of tissue serve best when placed within the advancing induration. Element needles serve practically the same purpose in most lesions. From 80 to 120 mg.-hr. or mc.-hr. per cubic centimeter of tissue is a fair estimate of the range of dosage. Cross-fire irradiation from surface application, using the beta ray screen, aids greatly in eradicating the disease. Lymphatics draining the area involved should be irradiated with deep external applications, whether or not palpable masses are present. If accessible secondary masses are found, interstitial application is valuable.

In carcinoma of the urethra interstitial application is best, being careful to avoid the lumen of the urethra by 0.5 cm. so as to maintain, if possible, its integrity and function. A retention catheter is often a necessity during the height of the reaction. Its use is probably less irritating than frequent catheterization over a painfully inflamed area. The implantation of the seeds or needles may often be done under local anesthesia. To avoid introducing added infection, the insertion should be made through uninvolved tissue when possible. Heavily screened tubes may be inserted within the urethra, keeping the dose sufficiently small to avoid a caustic action if possible. Distribution of the radiation along the urethra beyond the area of induration is advisable, keeping the dosage around 50 mg.-hr. per linear centimeter of lumen. This dosage depends, of course, upon the amount of interstitial radiation given. Lymphatics draining the involved area should be irradiated. For this purpose intense irradiation with an external applicator containing from 1 to 4 gm. of radium, at 6, 10, or 15 cm. distance, gives the best promise of success. Vaginal applications are often useful for cross-fire irradiation. Gamma ray applications kept 1 inch from the wall may be employed to the extent of 600 to 800 mg.-hr. without serious damage to the vagina.

Primary carcinoma of the vagina is rare. Surface applications, employing beta rays plus gamma rays, or gamma rays only, serve best when the involvement is superficial. When the induration is deep, interstitial application may well be employed with safety. The dosage will depend upon the

depth to which the lesion has infiltrated. If the lesion is 0.5 cm. or more in thickness, gold implants of 1.0 to 2.0 mc. each, or radium element needles, with a total dosage of 80 to 120 mc.-hr. or mg.-hr. per cubic centimeter of tissue, should suffice. The dosage by the surface method may vary from 50 to 100 mc.-hr. or mg.-hr. per square centimeter of surface. Normal vaginal wall should be protected by pushing away with gauze packs, increasing the distance from the radium as much as possible. Cross-fire from the rectum should be employed when the posterior vaginal wall is involved. A total of 800 to 1000 mg.-hr. of gamma radiation may be safely given per rectum with 1.0 cm. distance. Applications may usually be repeated in from four to six weeks, depending upon the extent of caustic destruction resulting from the initial treatment. A second and even a third irradiation may be given, bearing in mind the lowered local resistance to irradiation on account of tissue damage in normal structures.

Reaction. The general reaction from radiation administered in carcinoma of the vulva, urethra, or vagina is ordinarily mild. When several gram-hours of treatment are given, the reaction will vary accordingly. Malaise, depression, nausea, and vomiting may follow. Ordinarily the general reaction is secondary to the local changes produced rather than to direct systemic effects of the radium applications. Locally the reaction begins within a week following interstitial irradiation. Inflammatory swelling, vacuolization, nuclear disintegration and liquefaction with sloughing are in progress during the latter part of the first and during the second week. The surface of the ulceration shows the disintegration and increased discharge most markedly by the end of the second week. In superficial lesions when dosage and technic are well adapted to the pathological condition, repair begins to be evident in the fourth week and is complete by the fifth or sixth week, new membrane covering the ulcerated area by the sixth. The healing is delayed when radon implants are used and when the lesion is thick. Sloughing continues until the malignant tissue is destroyed and disintegrated, or the slough has separated. When there are deep vulvar lesions, sloughing

may be deep with but little tendency to heal for several weeks. Slow healing is probably due to the areolar nature of the submucous tissues and their scant blood supply. Vaginal lesions heal more readily and rapidly. In urethral carcinoma the ulcerated area is usually smaller with more submucous induration and involvement. The products of destruction due to radiation in these cases are absorbed rather than discharged or sloughed from the surface. An increase in the proportion of absorption increases the general reaction.

The local reaction in urethral lesions is characterized by swelling and subsequent submucous disintegration, absorption, and contraction. The urethral canal may be blocked during the height of the reaction. By the fifth or sixth week the repair and contraction are accomplished but in extensive lesions it may be delayed longer. Acute pyogenic infections, especially in extensive ulcerations of the vulva, are not uncommon. They add greatly to the patient's discomfort; pain is increased; sloughing, and especially healing, are delayed and the local reaction is prolonged. Perineal cellulitis may further complicate the reaction. Hemorrhage is rare. Deep late sloughs may occur in vulvar or urethral lesions, due to local late necrosis. The end result, if the tissues have responded satisfactorily, is a smooth, scarred surface, free of induration. Later contractions with mild degrees of distortion and telangiectasis may follow in moderately extensive lesions. In carcinoma of the urethra, when local irradiation has been adequate, there is scarring at the site of the ulceration, and some distortion or constriction of the canal, with fibrous thickening of the area formerly involved. Recurrences are indicated by enlarging tumor masses, hypertrophic ulcerations adjacent to or at the site of the lesion, by the development of secondary growths in nearby lymph nodes, or by failure to destroy the peripheral portions of the growth by irradiation.

Prognosis. Early lesions of the vulva yield to adequate irradiation. Local eradication is often complete. In extensive lesions with metastases palliation only can be hoped for. To accomplish palliation the dosage may have to be reduced. In hopeless cases the production of deep sloughs with delayed

healing is of doubtful value. Only in lesions in which there is reasonable hope of local eradication should extensive destruction be attempted. The percentage of cures is small but the palliation in advanced cases, the inhibition of recurrences in recurrent cases, and the improvement in results in operated cases, when aided by irradiation, all enhance the value of radium in caring for this small but serious group of malignancies.

Case Histories

Mrs. T. Aged sixty. Carcinoma of the vulva. Raised, ulcerated, foul-smelling lesion on right labium, 10 by 6 by 3 cm. Inguinal adenitis. Wassermann negative. Application of 2400 mg.-hr. radium at 1 inch distance, beta ray screen, over glands; 2000 mg.-hr. with 100 mg. of radium in needles (emitting 13 per cent beta rays) in the mass. Total, 4400 mg.-hr. Raised mass reduced to deep sloughing ulcer. Some inhibition of inguinal induration. Indolence for few weeks, with gradual decline ending in death at ten months.

Mrs. F. Aged fifty-three. Squamous-celled carcinoma of vagina. Anterior wall of vagina chiefly involved, also to lesser extent cervix and posterior wall. Primary site in doubt. Radium, 100 mg. for twelve hours, with beta ray screen and 6 mm. distance applied against lesion at intervals of three weeks for total of four treatments, total dose amounting to 4800 mg.-hr. Reduction in mass, with general improvement but eventual extension anteriorly. Metastasis and death in one year.

Mrs. V. Aged forty-seven. Carcinoma of urethra. Ulcerating, foul, friable lesion involving urethral canal, anterior wall of vagina, and labia minora. Application of 50 mg. of radium, with beta ray screen, against the lesion for twenty-four hours. One month later, four needles, amounting to 50 mg., inserted into mass for twenty-four hours (employing 13 per cent of beta rays). Total dosage 2400 mg.-hr. Relief from pain was marked. Complete healing after slough. Urinary continence. Death from lesion one year later.

References

Aikins, W. H. B. The value of radium in malignant gynaecological conditions. *Canada Lancet*, 47: 742, 1914.

Aikins, W. H. Radium in the treatment of diseases of women. *N. York M. J.*, 116: 340, 1922.

Bailey, H., and Bagg, H. J. Effects of irradiation on fetal development. *Am. J. Obst. & Gynec.*, 5: 461, 1923.

Bailey, H., and Bagg, H. J. Vulval and vaginal cancer treated by filtered and unfiltered radium emanations. *Am. J. Obst. & Gynec.*, 2: 587 1921.

Bailey, H., and Quimby, E. The use of radium in cancer of the female generative organs. *Am. J. Obst. & Gynec.*, 3: 117, 1922.

Bertolini, G. Various histologic forms of cancer of the female genitals and their radio-active sensitivity. *Actinoterapia*, 3: 238, 1923.

BLAND, P. B. Radium therapy in gynecology. *Med. J. & Rec.* 120: 101; 156, 1924.

BOWERS, L. G., and ARN, E. R. The use of radium in general surgical conditions with special reference to uterine conditions. *Ohio State M. J.*, 17: 834, 1921.

CAMERON, G. S. Some uses of radium in diseases of women. *Canad. M. J.*, 13: 872, 1923.

CLARK, J. G. The surgical and irradiation treatment of benign and malignant growths of the uterus. *Internat. Clin.*, 1: 74, 1924.

CLARK, J. G. The relative values of radium and surgery in the treatment of tumors of the pelvic organs. *Ann. Surg.*, 71: 683, 1920.

CULVER, H., and FORSTER, N. K. Primary carcinoma of the urethra. *Surg., Gynec. & Obst.*, 36: 473, 1923.

CURTIS, A. H. Special features of radium therapy in gynecology. *Wisconsin M. J.*, 21: 498, 1923.

DAELS, F. The radiation of the true pelvis with the help of drainage tubes. *Arch. Radiol. & Electroth.*, 27: 257, 1923.

DANFORTH, W. C. The use of radium in gynecology. *Illinois M. J.*, 49: 80–83, 1926.

DEGRAIS, P. Curietherapy (radiumtherapy) in vulvar vegetations during pregnancy. *Canad. Pract.*, 47: 47, 1922.

FITE, W. P. Radium as an adjunct to surgery in uterine conditions. *J. Oklahoma M. A.*, 16: 182, 1923.

FRANKL, O. X-ray and radium treatment in gynecology. *Dublin J. M. Sc., incl. Tr. Roy. Acad. Med. Ireland*, 4. S., 500, 1921.

GARIPUY, R. Cancer of the vagina treated with radium during pregnancy. Disappearance of the tumor. Delivery in normal term. *Bull. soc. d'obst. et de gynec. de Paris*, 13: 553–554, 1924.

HARTMANN, H., and FABRE, S. Pregnancy. *Bull. soc. d'obst. et de gynec. de Paris*, 12: 167, 1923.

HOON, M. R. Solid carcinoma of the ovary. *Ann. Surg.*, 71: 775, 1922.

KEENE, F. E. The value of radium in gynecology. *New York State J. Med.*, 22: 1, 1922.

KEITH, D. Y. Radiation in pelvic disease. *Kentucky M. J.*, 20: 128, 1922.

KELLY, H. A. Radium therapy, with special reference to diseases of the female pelvis. A rejoinder. *Therap. Gaz.*, 46: 761, 1922.

KELLY, H. A., and BURNAM, C. F. Radium in the treatment of carcinoma of the cervix uteri and vagina. *J. A. M. A.*, 65: 1874, 1915.

KUPFERBERG, H. Seven years of treatment of gynecologic cancer. *Strahlentherapie*, 13: 88, 1921.

KUPFERBERG, H. Radium therapy of benign gynecologic diseases. *Strahlentherapie*, 14: 549, 1922.

LAFFONT, M. Large carcinoma of the anovulval region treated by radium. *Bull. soc. d'obst. et de gynec. de Paris*, 13: 250, 1924.

MAXWELL, A. F. Results of radium in gynecology. *California State J. Med.*, 21: 155, 1923.

MCGLINN, J. A. The value of radium in gynecology. *Therap. Gaz.*, 46: 609, 1922.

Mundell, J. J. Four years experience with radium in the treatment of gynecologic conditions. *Am. J. Obst. & Gynec.*, 10: 70, 1925.

Norsworthy, O. L. Radium in gynecology. *Texas State J. Med.*, 18: 370, 1922.

Novak, F. V., and Kostalkova-Novak, R. Radium treatment and dosage in gynecology. *Prakt. lek., Prague*, 4: 75, 1924.

Odescalchi, I. The present status of gynecologic radiotherapy. *Ann. di ostet. e ginec.*, 45: 605, 1923.

Pemberton, F. A. Childbearing after radium and x-ray treatment. *Surg., Gynec. & Obst.*, 39: 207, 1924.

Pheland, G. W. X-ray and radium therapy in gynecology. *Long Island M. J.*, 17: 224, 1923.

Pomeroy, L. A., and Milward, F. W. A case of primary carcinoma of the female urethra treated with radium. *Surg., Gynec. & Obst.*, 35: 355, 1922.

Pomeroy and Milward. Radium in lesions of the female urethra. *Am. J. Roentgenol.*, 12: 524, 1924.

Rushmore, S. Progress in gynecology. *Boston M. & S. J.*, 174: 277, 1916.

Schmitz, H. The action of gamma rays of radium on deep-seated inoperable cancers of the pelvis. *Chicago Med. Soc. Bull.*, 15: No. 42, 1916.

Schmitz, H. An additional contribution to the therapeutic value of radium in pelvic cancers. *Surg., Gynec., & Obst.*, 23: 191, 1916.

Schmitz, H. The action of radium on cancers of the pelvic organs. *J. A. M. A.*, 65: 1879, 1915.

Schmitz, H. Radium in gynecology. *Interstate M. J.*, 23: 1097, 1916.

Shaw, W. F. Carcinoma of the female urethra. *J. Obst. & Gynec. Brit. Emp.*, 30: 215, 1923.

Shoemaker, G. E. Primary carcinoma of the urethra, retention of urine from obstruction, restoration of function by radium. *Surg., Gynec. & Obst.*, 22: 730, 1916.

Skeel, R. E. Modification of the indications for operative interference in gynecology imposed by present day radium therapy. *Northwest Med.*, 21: 131, 1922.

Stacy, L. J. The treatment of primary carcinoma of the vagina with radium. *Am. J. Roentgenol.*, 9: 48, 1922.

Sweetser, H. B. Radium versus surgery in gynecology. *Journal-Lancet*, 41: 637, 1921.

Tsakona, S., and Kopp, J. The use of radium in gynecology. *Rev. franc. de gynec. et d'obst.*, 17: 145, 1922.

Williamson, H. C. The indications and limitations of irradiation in obstetrics and gynecology. *New York State J. Med.*, 23: 341, 1923.

PART IV

MISCELLANEOUS TUMORS AND CARCINOMATA

MISCELLANEOUS TUMORS AND CARCINOMATA

Sarcoma (bone)

Diagnosis is not discussed in this outline, but should be established by roentgen-ray study and by biopsy if feasible, in every possible instance. (See p. 13.)

Pathology. Sarcoma of bone is most commonly of the small round-celled or spindle-celled type, and more often originating in the periosteum than in the shaft. The cells are of the rapidly growing, undifferentiated, infiltrative types. The tumors are vascular. They spread by the blood stream more often than by lymphatics. Periosteal lesions may extend around or along the shaft of the bone and into the adjacent soft tissues. Central sarcoma destroys the bone and may burrow through to the periosteum. A not uncommon development is the formation of a cyst resulting in spontaneous fracture. The degree of malignancy is high. The long bones are most frequently attacked. Tumors consisting of round-celled and of spindle-celled types merged with other types of tissue, such as cartilage, fibrous tissue, and mixed cells, present variable degrees of malignancy.

Radium Indications. Radium radiation is well adapted to cause degeneration of the malignant cells of small round-celled and spindle-celled sarcoma of bone. Radium rays, when homogeneously and efficiently distributed throughout a lesion of this sort, are theoretically capable of completely destroying all malignant cells therein. However, the mechanics of the applications are so difficult and fraught with so much danger that the successful eradication of the disease is rarely, if ever, accomplished. The interstitial application offers the best hope of cure. Interstitial application means mechanical penetration into the interior of the tumor with the inevitable accompanying danger of opening up avenues for spread of the disease, and of actually breaking off portions of the malignant growth and sending them on their way to distant parts of the body to hasten the fatal outcome, regardless of successful results locally. The

palpable border of the growth is probably not the actual margin and these frontier cells are best able to promote dissemination and resist the action of the rays.

Deep external irradiation averts the danger of mechanically induced metastasis, but it involves the disadvantage of being obliged to operate through normal structures whose integrity must be preserved. Cross-fire applications from many portals of entry enable greater concentration of rays within the tumor than at any point in the normal tissue, especially when the long bones of the extremities are involved. Cachexia contraindicates treatment, except in extreme cases, where, for special reasons, treatment must be resorted to as, for example, for the relief of pain. A hemoglobin reading below 50 per cent or a leucocyte count below 3500 contraindicates further treatment, lest the patient die from the treatment rather than from the disease. Distant secondary growths contraindicate anything but efforts to produce the simplest palliation.

The *contraindications* and *dangers of* radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Interstitial applications can be made through the skin, employing strongly built element needles. Careful mensuration or control by roentgenogram or fluoroscope is necessary to insure homogeneous distribution. From 100 to 130 mg.-hr. per cubic centimeter of tissue is a justifiable dose when one takes care to avoid large blood vessels and nerve trunks. Gold implants may be employed, carefully controlled by the fluoroscope and mensuration as to number of implants and depth of insertion. Gold implants containing from 1.5 to 2.5 mc. of emanation are justifiable. Unless homogeneous distribution can be obtained throughout the mass and for 1 or 2 cm. beyond the palpable margin, especially proximally, the interstitial method of application is not advisable except as a palliative measure. Central sarcoma defies interstitial insertion of radium through the skin. Open operation with gross exposure is then required to accomplish this type of application. Again, when periosteal sarcoma invades the diaphysis, open operation is necessary if interstitial application is to be

made. Necessary applications may be repeated in three months. Open operation to insert radon seems unjustifiable.

An external application of deep irradiation is the least dangerous form of radium therapy. If the extremities are affected, a cross-fire technic greatly increases the efficacy of the treatment. In the average case the lesion may be surrounded with radium in dosage of 1000 to 1200 mg.-hr. of gamma rays, at 1 inch distance over each 2 sq. in. of skin surface, without danger to the skin. Intense irradiation with an applicator containing from 1 to 4 gm. at 6, 10, or 15 cm. distance probably gives the best promise of success. Complete destruction by autolysis may thus be attempted. Treatments may be repeated in four weeks, governed by the skin reaction to the previous treatment, and adjusted to the changes in the tumor mass as observed clinically and by roentgenograms. Prior to any radium treatment of bone sarcoma, careful roentgenologic examination of the whole body should be made, to rule out the presence of any secondary growths. Secondary growths contraindicate any but the simplest palliative treatment. Inhibition of the growth may often be accomplished by deep external irradiation. Thus, death by distressing mechanical encroachment upon vital structures may be avoided, and the patient permitted to succumb to cachexia and wasting. In many cases pain may be controlled by a dosage insufficient to cause necrosis. Central breaking down, extensive ulceration and invasion of vital structures may be inhibited by palliative dosage. Treatments may be given in divided doses by the deep external method, being careful not to subject the same skin area to heavy irradiation more frequently than once every four to six weeks. The total dosage may reach many gram-hours, as high as 100 or more gram-hours being administered over a period of months or years.

Reaction. Often the general reaction from heavy irradiation, either interstitial or deep, is severe. Malaise, nausea, vomiting, anorexia, even diarrhea, follow irradiations of 15 to 20 gm.-hr. given within a few days. Free ingestion of fluids orally, rectally, and in severe reactions subcutaneously, are required to combat irradiation sickness. Preliminary blood transfusions, as well as transfusions during and

following the treatment, are often indicated. The general reaction continues as long as there is destruction and absorption of malignant tissue. Many weeks may be required for the patient to convalesce from the treatment alone, regardless of the effects of the disease itself. Such patients should be hospitalized under close observation and competently treated with all supportive measures available.

Locally, the reaction begins within a week when interstitial irradiation is employed. Inflammatory swelling begins early. If there were at the outset symptoms due to pressure, these symptoms are apt to be increased. After the first few days of inflammatory swelling the disintegration and absorption of malignant cells are evident. By the third week absorption has proceeded to a sufficient degree to result in decrease in size of the tumor mass and relief of pressure symptoms. Complications in the form of secondary pyogenic infection are distressing and may be serious. Abscess formation with spontaneous or surgical drainage occasionally occurs, with sinus formation and a resulting protracted course toward healing. If, at the end of six weeks, the mass has become quiescent, the reaction may be considered as complete. Further gradual shrinkage may occur; however, a more likely occurrence is the beginning of re-growth, or the appearance of adjacent extensions or more distant secondary masses. The recrudescence of the local growth indicates re-treatment after the sixth or eighth week.

Deep external irradiation results in a somewhat delayed and more gradual reaction. The onset of the local inflammatory swelling may not appear until the latter part of the second week. The swelling is more gradual though it may be greater than with the interstitial type of application. Autolysis is in progress in the third, and is probably completed by the end of the fifth week. By the sixth week there should be a marked reduction in the size of the mass if treatment has been adequate and the tumor is at all susceptible to irradiation. Increase in size of the treated mass or of adjacent masses may appear by the seventh or eighth week, or it may be delayed many weeks. Continued shrinkage is encouraging. Regrowth indicates renewal of the treatment, heavier or lighter, according to the reaction of

the skin and tumor mass to the initial treatment. Favorable termination is rare though the mass may shrink to a negligible quantity of fibrous tissue which remains quiescent for many months, rarely years.

PROGNOSIS. Practically all bone sarcomata terminate fatally under any form of treatment. Adequate radium treatment in many cases undoubtedly postpones the fatal day. Relief from pain, erosion, or invasion of vital structures, and inhibition of the growth are accomplished, and the end made more tolerable in a majority of the cases by the adequate use of radium.

CASE HISTORY

Mr. A. Aged twenty-four. Osteosarcoma of femur. Indurated, painful, nonulcerated swelling, middle half of right thigh. Roentgenograms show involvement of bone with fusiform swelling. Has had roentgen-ray therapy and Coley's serum. Had 4000 mg.-hr. radium therapy externally at another clinic. Treatment: 100 mg. radium in needles, inserted homogeneously through induration for eighteen hours, totalling 1800 mg.-hr. at one sitting, and 1200 mg.-hr. at another sitting. Also, 12,500 mg.-hr., externally, with beta ray screen, at 1 inch distance, at various sites surrounding lesion. Duration of treatments three months. General improvement marked as regards anemia, pain, reduction in size of leg. Roentgen-ray findings became practically normal. Eventual regrowth and death in eighteen months.

REFERENCES

BISSELL, J. B. Bone sarcoma treated by radium. *N. York M. J.*, 104: 3, 1916.

CASTERAN, E. Necrosis of bone and cartilage following radium therapy. *Rev. de especialid.*, 3: 70, 1928.

EWING, J. A review and classification of bone sarcoma. *Arch. Surg.*, 4: 485, 1922.

EWING, J. Radiation osteitis. *Acta Radiol.*, 6: 399, 1926.

HERENDEEN, R. E. Diagnosis and results in the radiation treatments of some medullary bone tumors. *Radiology*, 7: 140, 1926.

HOFER, G. Late occurrence of bone sequestration following radium therapy. *Wien med. Wchnschr.*, 77: 1037, 1927.

NEILL, W., JR. Radium in the treatment of sarcoma and carcinoma of the bone. *Am. J. Surg.*, 35: 32, 1921.

PHEMISTER, D. B. Radium necrosis of bone. *Am. J. Roentgenol.*, 16: 340, 1926.

REDER, F. The tragedy of a sacral periosteal sarcoma. *Am. J. Obst. & Gynec.*, 5: 266, 1923.

CARCINOMA OF THE BREAST

Diagnosis is not discussed in this outline, but should be established by biopsy whenever doubt exists. (See p. 13.)

Pathology. Glandular carcinomata, variously indicated as medullary, carcinoma simplex, or scirrhous, according to the preponderance of cellular content, are commonly

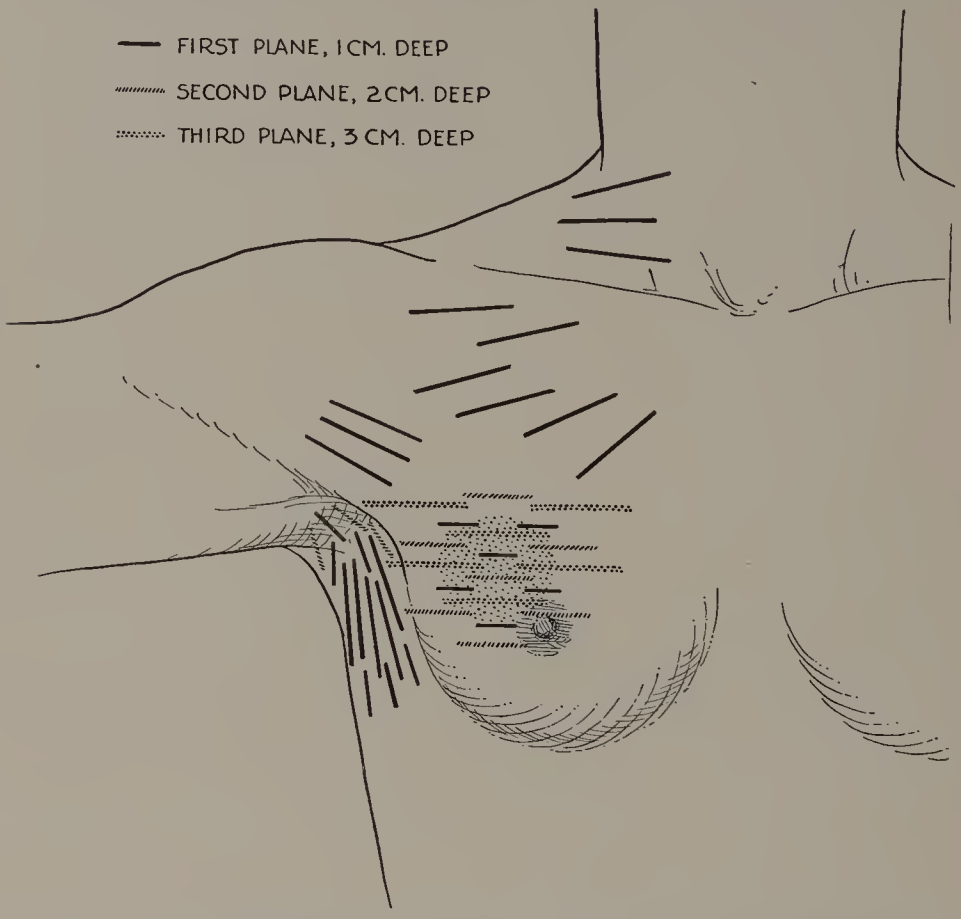


Fig. 25. Typical Radium Application in Breast Carcinoma. Primary growth and chief efferent lymphatic nodes implanted with radium needles of 0.5 mm. platinum wall and containing 1 mg. radium per centimeter of length. Dosage 96 to 120 mg.-hr. per linear centimeter.

found in the mammary gland. The growth develops within the breast tissue and infiltrates the ducts and fatty tissue early. The skin becomes adherent and dimpled, and in centrally located lesions the nipple becomes retracted early. The lesion extends in all directions, ultimately involving the skin and the entire gland, as well as the underlying muscles. In the medullary type, secondary growths develop early, involving the axillary lymph nodes and both the infraclavicular and the supraclavicular lymphatics. The mediastinal glands, the pleura, the opposite breast and the distant

skeleton may become the site of metastatic growths. There is marked variation in the progress of the disease, depending upon the cellular content of the lesion and upon the age of the patient. Generally speaking, the greater the preponderance of cellular content over fibrous tissue, the more rapid is the progress. Only a biopsy will establish the diagnosis in early cases.

Radium Indications. Radium is well adapted for the treatment of carcinoma of the breast at any stage. The lesion is readily accessible for application and observation. Ordinarily no vital structures interfere with adequate irradiation. Complete eradication or arrest by inhibition of malignant proliferation is possible in a large proportion of the cases. Secondary growths are most to be feared. In many such instances radiation is all that can be relied upon. In extensive cases and in recurrences, interstitial and intensive deep external irradiation give greatest relief. Preoperative and postoperative irradiation are valuable, the latter probably more so than the former. Accessible recurrent nodules yield under radium. Distance and inaccessible secondary lesions usually constitute insurmountable obstacles to treatment. Early primary growths are universally treated by radical excision. Supplementary irradiation undoubtedly improves the results, whether given before or after excision. Borderline cases require the aid of radium in sealing lymphatics, inhibiting growth and in preventing extensions and recurrences. In the inoperable cases radium is indispensable if any real attempt is to be made to secure palliation. The power of radium to necrose and inhibit the progress of malignant growths of the breast is unsurpassed.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Operable cases may be treated preoperatively by deep external irradiation to advantage. The fields treated should include the primary lesion, the axilla, the clavicular lymphatics, in fact, all efferent lymphatics of the breast. A standard of screening distance and milligram-hour dosage must be selected according to the amount of radium available. Three weeks later interstitial irradiation of the local lesion is advisable. Element needles or radon

implants should be inserted in sufficient amount to destroy local malignant tissue. Gold seeds containing 1 to 2 mc. each, distributed one per cubic centimeter of tissue or 100 to 120 mg.-hr. of 10 per cent beta ray needle radiation may serve as a standard. Local intradermal anesthesia usually suffices for the insertion. Operation is probably best done six weeks after the interstitial irradiation. This type of irradiation is not commonly carried out because its advisability has not gained credence. Many factors are responsible: the surgery is delayed, and such a large dosage of radium is expensive. The method has not been employed sufficiently to demonstrate that the superior results obtained justify this rather elaborate treatment. As a rule, the operable cases receiving radium treatment obtain it postoperatively, which is better than no irradiation at all.

External irradiation applied over the whole operative field and the efferent lymphatics is advisable. Gold implants buried permanently at sites of special susceptibility or capsules of radium buried in the base of the wound at the time of operation inhibit recurrence. Heavily screened, rubber covered applicators are buried deeply in sinuses left for the purpose. Gradual withdrawal produces irradiation of each segment as desired. Five hundred milligram-hours per 2 linear inch segment with beta ray screen and 3 mm. of rubber may be used with safety. Borderline cases, if inadvertently operated upon before irradiation, constitute urgent indication for radical radium therapy. Palpable recurrent nodules are best treated interstitially, with implants or element needles. One to 2 mc. gold seeds or approximately 120 mg.-hr. per cubic centimeter of tissue from 10 per cent beta ray needles should be sufficient.

Deep external irradiation over the operative field and the efferent lymphatics will inhibit incipient growth which might otherwise develop rapidly. It is the distant and inaccessible secondary lesions that are most to be feared. All inoperable cases, except those *in extremis* or showing cachexia are satisfactorily treated by external irradiation over the involved and efferent lymphatic areas. Three weeks later interstitial applications are made to accessible nodules as indicated. Dosage should be full in breast lesions. In

axillary and clavicular masses the proximity of large vessels and nerves must be kept in mind. Interstitial applicators must not be placed nearer than 0.5 cm. to vital structures on account of possible damage from their caustic action. In making external applications to irregular surfaces, such as the axilla and the cervical regions, care must be taken that the skin of the arm, neck, or other member which might come in close contact with the radium, be kept at a sufficient distance from the capsule on all sides to prevent damage. A cylindrical applicator of balsa wood, having a radius of the distance required for the application, protects surrounding soft parts from too close proximity to the radium. Careful blocking out of the area, accurate application and retention, coupled with caution as to overlapping of irradiated areas, are urgently required.

External irradiation by a block method is commonly practised in European clinics in cases of advanced cancer of the breast where there is extensive ulceration, fixation to the chest wall, and with secondary nodules in the axillary and clavicular regions. Tubes containing 20 mg. each are placed 6 cm. from the skin and 6 cm. apart over the whole mammary and secondarily involved areas for a period of ten days of continuous radiation. The screen is 1 mm. of platinum, or the equivalent, and the blocks are of wood or a paraffin-wax combination. Total dosage reaches to 50,000 to 100,000 mg.-hr. The radium is removed daily with its light wooden or modelling compound carrier and inspection made. If the temperature goes above 101.5°F. or the leucocyte count falls below 3500, the radium is temporarily removed.

Intense irradiation with an applicator containing from 1 to 4 gms. of radium at 6, 10, or 15 cm. distance may be applied over the efferent lymphatics draining the area. Such treatment probably gives the best promise of success. Subsequent interstitial applications may be made as nodules appear elsewhere in the field. Deep external applications may be repeated in six weeks, having due regard to the increased fibrosis and the decreased vascularity of the tissues.

In some instances platinum needles containing 1.33 mg. radium per linear 15 mm. and having a wall thickness of 0.5 mm. are inserted 1 cm. apart, and allowed to remain in

place seven days. Total dosage by this method may reach 3000 to 5000 mg.-hr. in the primary and secondary lesions.

It is probable that the roentgen ray has been used more extensively than radium in breast lesions. This has been true because of the economic aspect of the problem rather than because of demonstrable superiority of the roentgen ray over radium. Radium rays in sufficient amounts will accomplish results superior to those now accredited to the roentgen ray, probably because of their greater penetrability.

Reaction. Increasing amounts of external irradiation over the thorax result in general depression, malaise, anorexia, nausea and vomiting in proportion to the amount given. Leucopenia and anemia may follow excessive dosage. The general depression begins during the treatment and lasts for several weeks, being more marked if there is much destruction and absorption of malignant tissue. Supportive measures, such as increased fluid intake, tonics, forced feeding, and in extreme cases blood transfusion, greatly improve the end results. Blood transfusion may be given as a preliminary measure if the irradiation is to be heavy, and repeated during the reaction if indicated. By the sixth or seventh week the general reaction is subsiding but the patient should be supported and treated as one would manage a convalescent from a serious illness. The patient is ill. Locally, the reaction from external irradiation ordinarily consists of shrinkage of the malignant mass, or drying and healing of the ulcerated area, within three to five weeks.

Local necrosis by autolysis reduces the swelling, and fibrosis causes further contraction. Complete disappearance of all palpable nodules is uncommon. Some fibrous tissue always remains. Interstitial applications further reduce the indurated swellings, nodules or lymph-node involvements to a fibrous shrunken residue in the majority of instances. Skin reactions to the degree of epilation, erythema, scaling, or even ulceration may occur when deep external irradiation is pushed to the limit. Deeper ulcerations may occur from cross-fire or inadvertent overlapping of irradiated areas. However, they usually heal in three or four weeks with crust formation. Pleural irritation occasionally results from heavy deep irradiation. A temporary bronchial cough may

indicate even deeper untoward effects from the heavy irradiation.

Interstitial application to extensively indurated masses may result in rather extensive sloughing. Large ulcerations are to be avoided, if possible. Smaller nodules disappear within three weeks, leaving a fibrous remnant but a fraction of the original size of the nodule. Satisfactory end results present a quiescent operative field and neighboring lymph nodes free from active growth. Unfortunately weeks and months bring to light distant metastases or distressing recurrences which seem to have gained immunity against subsequent irradiation. Occasionally the radiologist comes upon a fulminating lesion, most often in women under forty, which progresses with distressing rapidity in spite of heroic efforts. Such instances furnish food for thought.

Prognosis. The prognosis must be guarded, even in the most favorable cases. The utmost variety exists in the clinical course of carcinoma of the breast, from acute, irrepressible fulminating growths to those very slowly growing scirrhous lesions in late adult life which persist for years without destroying the patient. Only careful clinical observation over long periods of time with accurate and complete pathologic data will finally permit an evaluation of the rôle of radium in carcinoma of the breast. Radium, because of demonstrated ability to destroy local lesions and its recognized power to inhibit extensive breast growths, should be employed to the utmost in aiding surgery or other measures in the uphill fight against this all too common invader.

Case History

Mrs. G. Aged seventy-four. Carcinoma of breast. Indurated mass in breast, present for five years. Adhesions to skin, causing retraction and slight ulceration of skin. No palpable secondary nodes. Size 6 by 6 by 4 cm. Treatment: 100 mg. radium for twelve hours in 8 needles (13 per cent beta rays). Reduced to a fibrous remnant in five months. Clinically well three years later.

References

Boggs, R. H. Ante-operative radiation of carcinoma of the breast. *Am. J. Roentgenol.*, 9: 508, 1922.

Bowing, H. H. Radium and x-ray treatment of advanced carcinoma of the breast prior to amputation. *Radiology*, 2: 143, 1924.

Cassidy, W. J. Carcinoma of the breast. *J. Michigan M. Soc.*, 22: 83, 1923.

De Backer. The radium-roentgen-surgical treatment of cancer of the breast. *Progrès. méd.*, 39: 522, 1924.

Kelly, H. A., and Fricke, R. E. Problems in treatment of carcinoma of the breast. *Surg., Gynec. & Obst.*, 38: 399, 1924.

Kirkendall, B. R. Radium in the treatment of carcinoma of the breast as an adjunct to surgery. *Am. J. Roentgenol.*, N. S., 8: 668, 1921.

Lee, B. J. Results of the treatment by radiation of primary inoperable carcinoma of the breast. *Ann. Surg.*, 76: 359, 1922.

Lee, B. J. Treatment of recurrent inoperable carcinoma of the breast by radium and roentgen ray. *J. A. M. A.*, 79: 1574, 1922.

Lee, B. J. Results and technic in the treatment of carcinoma of the breast by radiation. *Am. J. Roentgenol.*, 10: 62, 1923.

Lee, B. J., and Herendeen, R. E. The treatment of primary inoperable carcinoma of the breast by radiation. *Radiology*, 2: 121, 1924.

Levin, I. The prognostic and therapeutic significance of skeletal metastases in carcinoma of the breast. *Ann. Surg.*, 65: 326, 1917.

Mallet, L., and Coliez, R. Surgery, the x-ray, and radium in the treatment of cancer of the breast. *Arch. d'électric. méd.* 33: 31, 1923.

McCullough, J. F. Results of radiological treatment of carcinoma of the breast. *Radiology*, 4: 395, 1925.

Moore, J. T. Cancer of the breast. *Texas State J. Med.*, 18: 352, 1922.

Neuman, et al. Roentgen and surgical treatment of mammary cancer. *Arch. d'électric. méd., etc.*, 34: 33, 1924.

Perussia, F. Roentgen rays and radium in treatment of mammary carcinoma. *Radiol. med.*, 9: 493, 1922.

Pfahler, G. E. The treatment of recurrence and metastases from carcinoma of the breast by means of radium and roentgen rays. *Am. J. Roentgenol.*, 7: 328, 1920.

Pfahler, G. E. Radium combined with x-ray treatment in carcinoma of the breast. *Am. J. Roentgenol.*, 8: 661, 1921.

Pfahler, G. E., and Widmann, B. P. Statistical study of radiation therapy in eight hundred and one cases of carcinoma of the breast. *Am. J. Roentgenol.*, 14: 550, 1925.

Pfahler, G. E., and Widmann, B. P. The relative value of various technics in the radiation treatment of carcinoma of the breast. *Radiology*, 6: 493, 1926.

Roux-Berger, J. L. The association of surgery, x-rays, and radium in the treatment of carcinoma of the breasts, tongue, and uterus. *Paris méd.*, 13: 269, 1923.

Schmitz, H. The end-results of the treatment of carcinoma of the breast with surgery, radium, and roentgen rays. *Am. J. Roentgenol.*, 12: 531, 1924.

Stevens, J. T. Modern methods in the treatment of cancer of the breast. *Radiology*, 2: 156, 1924.

Tousey, S. A case of disseminated carcinoma of the breasts and axillae improved by radium. *J. A. M. A.*, 62: 1167, 1914.

Webster, J. H. D., et al. The treatment of fifteen cases of operable carcinoma of the breast by radium and x-rays. *Brit. J. Radiol.*, 31: 59, 1926.

Willis, G. S. Radium in carcinoma of the breast. *N. York M. J.*, 117: 453, 1923.

Endothelioma (nose and brain)

Diagnosis is not discussed in this outline but should be established by biopsy whenever feasible. (See p. 13.)

Pathology. As a rule, these rather uncommon neoplasms arise from the endothelial linings of blood vessels, from the meninges, or from lymphatics. The cells are of slow growth and are interspersed with a connective-tissue framework of doubtful origin. The common sites are about the nose and mouth and the meninges. Vascularity varies from none on the one hand, merging into angioma, almost wholly of blood-vessel structure, on the other. They give rise to symptoms chiefly by mechanical means, as by pressure, or by small hemorrhages. Erosion by pressure, with accompanying pain, is not uncommon in the air passages. Obstruction is frequently the first sign of their presence. Disturbance of nerve function accompanies the lesions involving the nervous system. Metastasis is rare. The tumors are more often circumscribed than infiltrating.

Radium Indications. Radium rays have almost a specific action on endothelial tissue. Relatively small doses are sufficient to cause complete disappearance with fibrous tissue replacement. Ordinarily the gamma rays, if efficiently applied, are sufficient to cause autolytic absorption without the caustic action of heavy exposures or of beta ray action.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. In general, the interstitial form of application is most desirable. Caustic action is best avoided by employing applicators so screened as to allow few if any of the beta rays to penetrate the tissue. Markedly vascular tumors are best treated without the insertion of radium into the tumor. Lesions in the nose and mouth, when of considerable size and accessible, are well treated by needles of sufficient screening power to absorb 95 per cent of the beta rays, or by the use of gold implants. Homogeneous distribution to the extent of 75 to 120 mg.-hr. per cubic centimeter of tissue usually serves very well. If interstitial treatment with screened radium is impractical, the tube with a beta ray screen may be employed as a surface or cavity application.

In tumors measuring less than 1 to 2 cm. a dosage of from 200 to 500 mg.-hr. with 2 to 4 mm. distance if possible, yields the best results. Such treatments are probably best given in divided doses from two to six weeks apart, continuing the treatment as the changes in the lesion indicate. Intracranial endothelioma may be treated by interstitial application at the time of exploration, employing gold implants of radon, the dosage probably best kept under 1.0 to 1.5 mc. per cubic centimeter of tissue. Repetition of the application seems unjustifiable. Deep external irradiation with gamma rays to intracranial lesions may supplement or supplant the interstitial method. Intensive irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10, or 15 cm. distance over several portals of entry probably gives the best promise of success. Cross-fire from many portals of entry is likely to be useful. Twelve hundred milligram-hours with beta ray screen at 1 inch distance over each 2 sq. in. of skin surface constitutes a fair dosage. It will produce complete temporary epilation. Dosages of this sort may be repeated in six or eight weeks, and be continued as symptomatic changes indicate. Recurrences in mouth and nose lesions are not uncommon but repeated irradiations reaching all parts of the lesion with the gamma ray will often clear up the condition.

Reaction. The general reaction is mild, since the dosage is usually not heavy. Malaise, with occasional nausea and vomiting, occurs. This reaction subsides in a few days, but may recur during the latter part of the second and early in the third week.

Locally, the reaction begins within ten days when the interstitial method is used. Inflammatory swelling, pain, and difficulty in swallowing or breathing, as the case may be, follow one another in order. After the second week the inflammation begins to subside and the tumor shrinks. Such shrinkage may continue for many weeks. Re-treatment is contraindicated as long as improvement continues. Gamma ray applications, unless very heavy, result in slower growth, less swelling, more gradual and prolonged shrinkage. When there is no visible local reaction, treatment may be repeated, employing heavier dosage until demon-

strable changes are noted. In mouth lesions the principal part of the reaction is over in six weeks, but continued improvement from a single treatment may endure for a much longer time. Increase in the size of the mass or a tendency to spread peripherally indicate the need of re-treatment. Successful treatment results in disappearance of the lesion with atrophy of the mucous membrane and dryness of the part; and, if the reaction has gone on to ulceration, white scar tissue will be present over the site. Brain lesions by analogy should yield, shrink, and disappear, leaving scar tissue in the site, and the symptoms caused by pressure should be relieved.

Case History

Miss P. Aged forty-five. Endothelioma of the nose. Smooth firm, friable, bleeding mass at site of left inferior turbinate, present for three years. Two needles of 25 mg. radium in lesion for one hour. Recurrence in six months. Then 50 mg. radium with beta ray screen, for twelve hours, totalling 600 mg.-hr., following partial curettement. No recurrence in three years.

References

Béclère, A. Radiotherapy of brain tumors. *Paris méd.*, 13: 97, 1923.

Edwards, D. J., and Bagg, H. J. Lesions of the corpus striatum by radium emanation and the accompanying structural and functional changes. *Am. J. Physiol.*, 65: 162, 1923.

Flatau, E. Radiotherapy of tumors of the brain and cord. *Rev. neurol.*, 1: 23; 176, 1924.

Pancoast, H. K. Treatment of brain tumors by radiation. *Am. J. Roentgenol.*, 9: 42, 1922.

Pinch, A. E. H. Endothelioma of the tongue. Report of Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, 2: 49, 1923.

Epulis

Diagnosis is not discussed in this outline, but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. This tumor is a not uncommon giant-celled fibrous growth, arising from the periosteum of the jaw. It is not highly malignant, growth is relatively slow, metastasis is rare, and ulceration late. The principal symptoms are due to the mechanical obstruction or to pain from pressure.

Indications. Radium rays are capable of completely destroying these mildly malignant tumors. They are usually readily accessible for treatment and observation. Several

methods of approach are available, namely, interstitial, surface or deep external irradiation with cross-fire.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The interstitial method of applying radium offers the best promise of good results. Element needles or radon implants may be employed, the dosage consisting of from 100 to 130 mg.-hr. per cubic centimeter if the element needles are employed, or 1.0 to 2.0 mc. per cubic centimeter if the gold implants are used. Surface application is often best when the lesion is superficial. In any case the periphery and surrounding 1 cm. of normal tissue should be carefully irradiated. Care must be taken to keep the radium 1 cm. away from the bone, lest radiation necrosis occur. Screened applicators may be placed against the surface of the mass, being held there in modelling compound. One must carefully push the tongue and cheek as far away from the radium as possible. One hundred to 130 mg.-hr. per square centimeter of surface is ordinarily sufficient dosage. The draining lymphatics may receive deep external treatment to the extent of 1000 to 1200 mg.-hr. per 2 sq. in. at 1 inch distance, using gamma rays only. This dosage may be varied, altering the milligram-hour dosage directly as the square of the increased distance. This is in accordance with the inverse square law. Second applications may be made eight weeks later for the treatment of recurrence, incomplete destruction, or extension. As in all instances, repeated radium applications are less effective.

Reaction. The general reaction as a rule is mild. After the interstitial application, the local reaction begins within a few days. Inflammatory swelling, necrosis and autolysis are at their height in the third week. The reaction usually subsides by the fifth. Ulceration is rare. Bone necrosis with sequestrum formation may occur if radium is placed too close to the bone. Ulceration may result when the surface method is used, though healing is often complete by the sixth week. A smooth, depressed scar presents in successful cases. Complete disappearance of the mass is rare, for the fibrous remnant of the growth persists. Metas-

tasis is unusual. Re-growth may appear from eight weeks on. Increase in size or extension to adjacent structures indicates recurrence. Delayed recurrences are rare.

PROGNOSIS. The prognosis is good because of the low degree of malignancy, and the accessibility of the lesion to direct treatment and observation. Efficiently treated cases usually respond with permanent cure.

REFERENCE

PINCH, A. E. H. Epulis of the jaws. Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, 2: 47, 1923.

CARCINOMA OF THE GALL-BLADDER, PANCREAS, AND SMALL BOWEL

Diagnosis is not discussed in this outline but should be established by roentgen-ray study and by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. In these structures, adenocarcinoma is practically the rule. The gall-bladder is infrequently the site of primary carcinoma arising usually about the neck of the gall-bladder or in the ducts, particularly the common duct. The majority of carcinomata of the small bowel are found at or about the ampulla of Vater; a few occur in the jejunum, ileum or appendix, but they are extremely rare. Primary carcinoma may occur in the head of the pancreas, though it is more often secondarily involved from lesions in the stomach or gall-bladder. Growth and extension of malignant tumors about the gall-bladder and ducts and about the pancreas are usually rapid. Symptoms of obstruction appear early when the gall-ducts are involved. Primary carcinoma of the gall-bladder is most often associated with gallstones. Often the lesion is discovered only at the time of laparotomy for gall-bladder pathology. Lesions in the head of the pancreas are usually extensive before arousing suspicion. If the ampulla of Vater is involved primarily, obstruction of both gall-ducts and intestines may result. These growths infiltrate rapidly, causing distortion and obstruction of the vital passages. They metastasize early to neighboring lymph nodes and to the liver. Peritoneal involvement appears early. Malignant lesions in these structures run a

short and destructive course with the possible exception of carcinoma of the neck of the gall-bladder. If the lesion is of the scirrhous type, the growth is slower and its symptoms are often only those of obstruction.

Radium Indications. In selected cases radium may be of some value. If a cholecystotomy is done and the carcinoma involves the neck of the gall-bladder or the duct so that excision is impossible, radium may be applied through the fistulous tract. Its inhibiting action may delay the progress of the disease. If the ducts are patent, capsules may be passed even to the ampulla, with some hope of palliation. In lesions involving the head of the pancreas, the possibility of useful local applications of radium is doubtful.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Surface or cavity applications of radium may be made to the neck of the gall-bladder or into the common duct, even as far as the ampulla if patency permits. A capsule attached to a semirigid sound may be passed through the fistulous tract and the site of the lesion canalized. The radium should carry a beta ray screen which may have to be platinum so that the caliber will be sufficiently small to admit the radium. A thin-walled screen might be employed if the lesion is extensive and annular. Two hundred to 1000 mg.-hr. per linear 1 inch segment would probably encompass the limits advisable. Lesser amounts, or series applications, would perhaps be the wiser procedure when the capsule is inserted farther into the common duct or to the ampulla. Extraperitoneal application of radium within the abdomen to these lesions is fraught with danger in view of the risk of secondary infection when the local resistance has already been lowered by the disease. Extreme jaundice is probably a contraindication to any but the mildest local applications of radium. It is probably better to delay local radium applications by means of sounds until after complete recovery of the patient from the surgical procedure. Cross-fire from the external abdominal wall is indicated and may be given to the skin tolerance dose, depending on the general condition of the patient. One thousand milligram-

hours at 1 inch distance with a beta ray screen over each 2 sq. in. of surface may serve as a standard under ordinary circumstances. Intense irradiation with an applicator containing from 1 to 4 gm. of radium, at 6, 10, or 15 cm. distance, may be applied over the lesion, using many portals of entry. Such treatment probably gives the best promise of successfully palliating the disease.

When large amounts of radium are available, the distance, screening, and size of portals of entry must be reckoned accordingly. If the head of the pancreas is involved primarily, the interstitial implantation of radon seeds might be attempted at the time of laparotomy, supplemented later by external cross-fire radiation over the site of the lesion from many portals of entry. Subsequent treatments, properly applied, are hardly possible without laparotomy. If the biliary fistula is still patent, canalization may be tried but the radiologist is working in the dark. Applications to malignant lesions of the appendix or the small bowel are rarely indicated.

Reaction. The few reactions seen by the author have been severe. Nausea and vomiting, with refusal of all nourishment, have followed the application of radium capsules through a biliary fistula. External applications over the abdomen in these lesions cause no more reaction than for other conditions over the abdomen. Exception is seen when infection is present in the gall passages, and, unfortunately, infection is often present. When the patient has been weakened by stenosis of the passages and toxic absorption, then he is less able to withstand the reaction; even prostration may supervene. The reaction from moderate amounts of irradiation in early, selected, and mechanically favorable cases would probably be mild; at least, it would not contraindicate palliative radium treatment. The local reaction consists of inflammatory swelling during the first two weeks, with subsequent narrowing of the lumen and possibly complete stenosis. Peritoneal irritation from local application is probably unavoidable. Secondary infection may cloud and complicate the picture. The local reaction, on account of its secondary effects, probably can cause more general disturbance when applied to these lesions than in any other part

of the body. Recovery from the reaction should be complete in five or six weeks.

Prognosis. Early death ensues as a result of the disease. Palliation may be attempted in accessible cases. It is probable that heavy external irradiation over the abdominal wall offers the best hope of satisfactory palliative results with a minimum of risk.

Case History

Mrs. D. Aged sixty-three. Carcinoma of cystic and hepatic ducts. Hard, indurated swelling the size of an almond, surrounding ducts, found at operation for gall-bladder disease. Thirty-five milligrams radium passed through drainage tube applied for four hours, totalling 140 mg.-hr. Beta ray screen. Dose repeated in four days, totalling 280 mg.-hr. No immediate reaction. Five days after second application patient went into shock and died. Hemorrhage and gas bacillus infection found at postmorten examination.

Chronic, Non-specific Adenitis

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13)

Pathology. Enlarged glands included in this group have an indefinite or unknown etiology. They cannot be classed with Hodgkin's disease, lymphosarcomata, tuberculous glands or luetic glands; therefore, this group includes those cases of chronic glandular inflammation of indefinite etiology. The glands are hypertrophic and hyperplastic with increase in capsule and stroma according to the duration of the condition. As a rule, they do not invade or extend beyond the capsule; the glands may be discrete or in chains, and usually they are movable. The cervical nodes are the ones most often involved.

Radium Indications. Lymphatic tissues are especially susceptible to radium rays, and so the shrinkage and disappearance of these glands of obscure etiology often follow irradiation. The application is simple, practically without danger, and there are few contraindications except acute local inflammatory processes with pus formation and fever.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation is the method of choice, the simpler and the safer mode of attacking these glands. The dosage may vary from 500 to 1000 mg.-hr. of

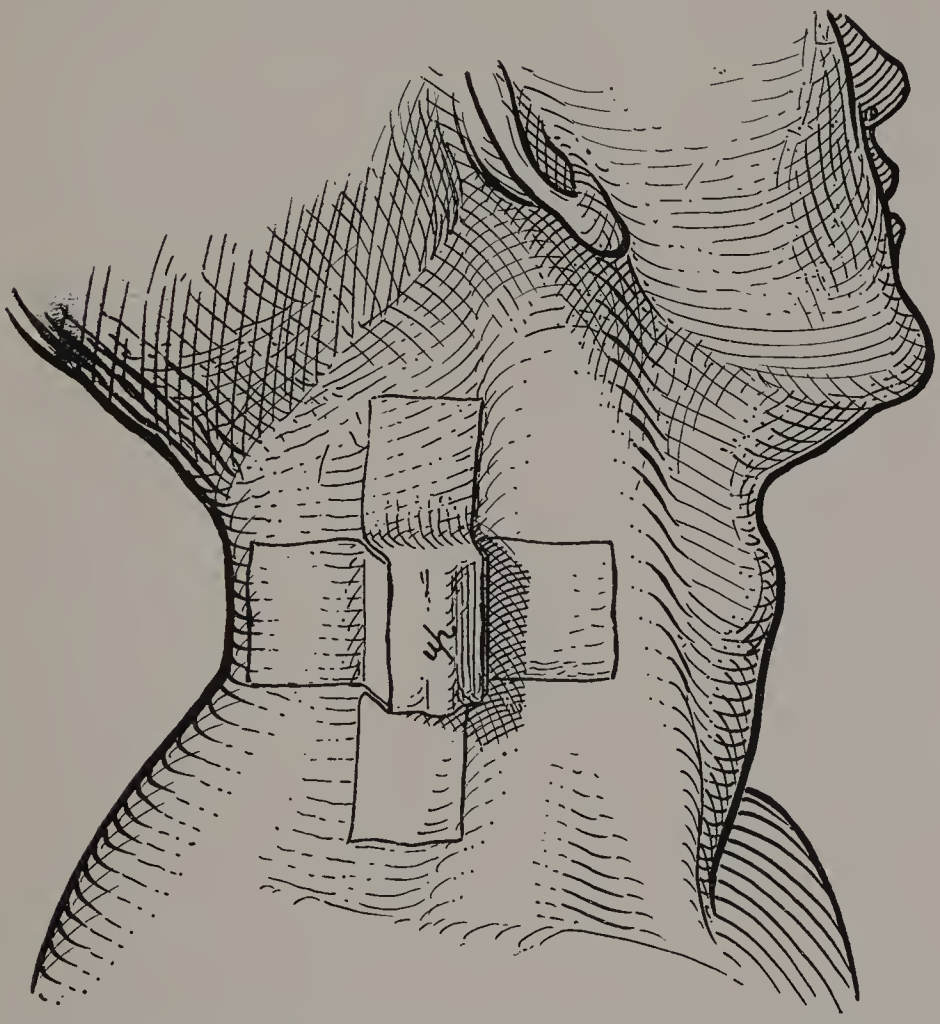


Fig. 26. Typical Radium Application in Enlarged Lymph Node of Neck. A 50 mg. radium tube applied at 2.5 cm. from skin over lesion. Dosage 1200 mg.-hr.

gamma rays at 1 inch distance for each 2 sq. in. of surface. Applications may be repeated four to six weeks later over the same area, and still once more if the condition remains unrelieved.

Reaction. The general reaction is usually mild unless the extent of involvement is great and the dosage required to irradiate all enlarged glands amounts to 10 or more gram-hours.

Malaise, anorexia, headache, and nausea with occasional vomiting, may begin during heavy dosage treatment, and it may continue for two or three weeks while the lymphoid tissue destruction is in progress. Locally,the reaction begins within a few days after treatment. The glands may swell but they soon begin to shrink as a result of the rapid destruction of the hyperplastic cellular glands. This decrease in size progresses rapidly so that in many cases by the third, or at the latest, the fourth week the glands may have completely disappeared or have been reduced to a fibrous stationary remnant. Favorable cases respond rapidly and completely to radium treatment, while some of the group of unknown etiologic factors, especially those of long standing, yield only to a moderate degree. Recurrences are uncommon. Glands which are reduced to an insignificant minimum, usually remain as such.

Prognosis. In glandular enlargements of unknown etiology in which the diagnosis of chronic adenitis seems to be as accurate as can be determined clinically, radium has so often caused a complete disappearance of these lesions that its use should not be overlooked. Its application is simple and its dangers practically nil, and the satisfaction which comes from a treatment which eradicates by means of simple radium application, thus avoiding surgical intervention, is certainly worth while. Complete clinical cure in these cases of chronic adenitis is almost the rule.

Case History

Mrs. P. Aged forty. Chronic adenitis. Enlarged nodes in right axilla, present one year following a skin infection two years previously. Sixty milligrams radium element, with beta ray screen, at 1 inch distance for twelve hours, totalling 720 mg.-hr. Liquefaction was evident three weeks after irradiation. Fluid removed by puncture drainage. Immediate recovery. No recurrence in eight years.

Reference

Pinch, A. E. H. Chronic lymphadenitis. Report of the Work at the Radium Institute, London, 1923. *Radium*, 3: 13, 1924.

Malignant Glands (metastatic)

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. Metastatic malignant glands are secondary growths, resembling the primary lesion as to cellular structure. Cells from the primary growth invade the gland by extension, permeation, or embolism. Their rapid growth causes early destruction of glandular structure, invasion of the capsule and infiltration of the adjoining structures. Central necrosis, skin invasion, softening with discharging sinus, or protrusion of a rapidly growing sloughing mass, are developments which follow one another in untreated cases. Vessels are invaded, hemorrhage is not uncommon, bone is invaded, the function of adjacent tissues is destroyed. This invading, destructive process leads to death by hemorrhage, perforation and fatal infection, or by widespread growth with toxemia, cachexia and death.

RADIUM INDICATIONS. Radium rays are capable of destroying malignant cells or inhibiting the growth of those not destroyed. Caustic necrosis or autolytic degeneration can be brought about by the action of radium radiation. The technic of the treatment is usually not difficult, and the danger is slight. Few contraindications to external treatment exist except cachexia. Interstitial treatment may be limited by proximity to vital structures, such as blood vessels of size.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. The interstitial, the cavity, and the deep external methods are available for the treatment of these secondary malignant growths. The interstitial method is the method of choice in glands which are completely accessible. Element needles or gold implants may be used. The implants in dosage of 1 to 2 mc. to each cubic centimeter of tissue (reduced to a slight extent centrally in amount on account of cross-fire from peripheral radiation) is a fair average dosage. Radiation should be applied as far as 1 cm. beyond the periphery of the mass, especially if the capsule is invaded. Seeds implanted at or just beyond the clinical margin to "hem in" the growth at its growing border are of the utmost importance. Element needles may be employed likewise, with dosage from 100 to 130 mg.-hr. per cubic

centimeter of malignant tissue. The interstitial method, unless heavily cross-fired by deep external irradiation, should include dosage 1 cm. beyond the clinical border of the disease equal to the amount given within the mass if efficient irradiation is to be secured.

Cavity irradiation may be used in instances of discharging sinuses by inserting, into the sinus, tubes screened or unscreened, with dosage of 600 to 1200 mg.-hr. per linear inch, if the sinus is completely surrounded by malignant tissue. Cross-fire by means of deep external irradiation, from all possible points, should supplement cavity treatment.

Deep external irradiation to the extent of 1000 to 1200 mg.-hr. per 2 sq. in. of surface at 1 inch distance, employing the beta ray screen, may be stated as a safe standard of dosage to employ, with variations to suit the individual circumstances. Intense irradiation with an applicator containing from 1 to 4 gm. at 6, 10, or 15 cm. distance probably offers the best hope of success. The irradiated area should include all involved glands and draining lymphatics in order to inhibit as much as possible the progress of the disease. Treatment may be repeated in four to eight weeks if the skin reaction permits. Ensuing treatments require gradually reduced dosage on account of increased skin susceptibility and fibrosis, and decrease in blood supply. A reduction of 25 to 50 per cent of the dosage, on account of the danger of breaking down the previously radiated and fibrotic area, is a wise precaution in repeating interstitial treatment to recurrences *in situ*. Deep external irradiation may be repeated advisedly several times at intervals of two to three months if the malignancy seems to be under control, and the general condition of the patient warrants it. Irradiation by means of implants, needles or tubes in the depth of the wound following surgical excision is good prophylactic therapy. The reduction of glands to a fibrous minimum after irradiation may permit complete surgical excision if the primary growth has been eradicated. In selected cases preoperative and postoperative irradiation probably offers the best hope of cure. In extensive hopeless secondary involvement it would be better to give inhibiting palliative treatment with careful estimation of dosage and

comparison of probable results with the probable course of the untreated disease. Cachectic patients probably should not be treated except for the express object of reducing masses causing dangerous obstruction or of diminishing bleeding, foul discharge and obnoxious sloughing ulcerations. Applications for palliation may be repeated at intervals of one month, but only when such treatment seems advisable in the individual case under consideration.

Reaction. The general reaction may be mild or marked, according to the magnitude of the dosage or the extent of tissue destruction. Malaise, anorexia, nausea, and occasional vomiting may follow heavy external irradiation to the extent of several gram-hours given within a short period of time. Extensive, interstitial treatment often results in marked general reaction. The blood count may be reduced. Local pain from swelling and inflammatory reaction may add to the general depression. Locally, following the interstitial treatment, the inflammatory swelling begins within a few days. Cellular swelling, disintegration, absorption or sloughing, and repair follow one another in order from the sixth day on to completion, usually by the sixth week. Deep external irradiation results in a reaction delayed perhaps until ten days, with autolysis and absorption continuing for three or four weeks, with the end results apparent by the sixth or seventh week. In favorable cases the masses shrink in six to eight weeks to a stationary fibrous remnant. Unfavorable cases may suffer a breaking-down with sloughing, necrosis and ulceration which may not yield for weeks and may later become the site of vigorous recurrences. Missed areas or portions failing to receive sufficient irradiation may recur in three or four weeks.

Prognosis. Secondary metastatic malignant glands are probably better treated by means of radium alone or in combination with surgical excision than by any other method. When secondary glandular metastases are present in malignant growths, the prognosis ordinarily is hopeless. However, one can bring about inhibition of the growth, and occasionally complete destruction of the secondary masses. Weeks and months of relative comfort may be secured for these patients. When the primary growth has been eradi-

cated, desperate effort should be made to eliminate, if possible, these secondary masses.

Case History

Mr. H. Aged sixty-eight. Malignant glands. Tumor, size of orange, on right side of neck, recurrent following operation for lip lesion thirteen years previously. Sinus, discharging foul debris. Treated by 2400 mg.-hr. at 1 inch distance over two areas with beta ray screen. Interstitial treatment refused. Symptomatic improvement only. Death six months later.

References

Hanford, C. W. Malignant glands and their proper treatment with radium. *Illinois M. J.*, 42: 214, 1922.

Janeway, H. H. The treatment of malignant tumors of the thymus gland by radium. *Ann. Surg.*, 71: 460, 1920.

Janeway, H. H. The use of buried emanation in the treatment of malignant tumors. *Am. J. Roentgenol.*, 7: 325, 1920.

Kurtzahn, H. The extent of applicability and methods of application of radium in the treatment of inoperable malignant tumors. *Strahlentherapie*, 13: 72, 1921–22.

Mottram, J. C. Some observations upon the histologic changes in lymphatic glands following exposure to radium. *Am. J. M. Sc.*, 165: 469, 1923.

Pinch, A. E. H. Lymphadenoma. Report of the Work at the Radium Institute, London, 1923. *Radium*, 3: 14, 1924.

Quick, D., and Cutler, M. Radiation reaction of metastatic squamous cell carcinoma in cervical lymph nodes. *Am. J. Roentgenol.*, 14: 529, 1925.

Rubens-Duval. The respective indications of surgery and radium in the treatment of operable malignant tumors. *Paris méd.*, 12: 85, 1922.

Stevens, R. H. The use of intravenous injections of radium chloride in some of the malignant lymphomata. *Am. J. Roentgenol.*, 16: 155, 1926.

Tuberculous Glands

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The lymph glands are enlarged, due to the chronic irritation of the tubercle bacillus; there is hyperplasia of the cellular structure, an increase in the capsule and stroma, the formation of typical giant cells, followed by caseation, softening, and often spontaneous discharge through a sinus. Following the discharge, the lesions usually dry, shrink to a fibrous remnant and finally heal, frequently with adhesions composed of scar tissue to the skin. The cervical glands are most affected, the axillary and the submaxillary glands less often. The skin is usually not involved,

except in cases of softening and breaking-down of the gland, with subsequent burrowing through the skin.

Radium Indications. The gamma rays from radium have repeatedly caused the shrinkage and disappearance of tuberculous glands. The action here is probably the alterative one, or perhaps the result of a local leucocytosis, rather than the direct effect upon the tubercle bacillus or upon the lymphoid hyperplasia. Prophylactic treatment is indicated after surgical excision or at the first sign of recurrence. The treatment is usually simple and observation of progress easy. No untoward effects result. Fluctuation and softening do not contraindicate radium treatment but if aspiration or puncture and drainage are needed, they should precede the radium treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation, employing gamma rays only, is the best method of applying radium to tuberculous glands. The dosage, the distance and the amount of radium used vary greatly with the radiologist and with the individual case at hand. Earlier stages of the disease require smaller dosage. A safe standard application employs gamma rays, at 1 inch distance, over each 2 sq. in. of skin surface in amounts from 200 to 1000 mg.-hr. per area during any month. Chronic, fibrous lesions of long standing require the higher dosage. It is probably best to begin with 200 to 500 mg.-hr. per 2 sq. in. at the outset and repeat this dosage at two to four week intervals, as the case indicates. In cases where there is extensive glandular involvement, it is perhaps advisable to keep the total dosage under 2 or 3 gm.-hr. per week. A few isolated, single glands may be irradiated vigorously with a dose of from 800 to 1000 mg.-hr. per area at the outset, each area covering a glandular mass. Many successes have been reported from the use of a few milligrams of radium (less than 25 mg. in amount) placed in flat applicators, applications being repeated twice a week, taking great pains in all instances to give less than the skin erythema dose, but extending the treatment over a long period of time. No matter what method is employed, the treatment should be

continued until the glands have disappeared, or until a stationary fibrous remnant remains.

Reaction. The general reaction is usually mild, consisting only of malaise. Locally, there may be a preliminary increased swelling of the glands, lasting for a few days, or the glandular mass may shrink rapidly without any preliminary swelling. Decrease in size often begins within ten days and continues until the fourth week. When the maximum dose is administered at the outset, complete disappearance may be accomplished in three or four weeks. With divided doses, given weekly or biweekly, the shrinkage is likely to occur more gradually. Occasionally softening and fluctuation appear. In such cases if spontaneous discharge is imminent, aspiration or small puncture drainage reduces the scarring. Favorable cases result in complete glandular disappearance or in reduction of the glands to a fibrous remnant. A few cases are somewhat resistant and require repeated applications. Rarely do tuberculous glands fail to yield to radium treatment.

Prognosis. In the majority of cases, tuberculous glands respond favorably to radium therapy; the earlier the stage of the disease, the more favorable the prognosis. Treatment is simple and practically without danger. A few cases experience softening and suppuration of the glands. No scarring or loss of tissue results. Radium therapy deserves wider employment in the treatment of tuberculous glands.

Case History

Mrs. M. Aged twenty-six. Tuberculous cervical glands. Gland in left cervical region, 4 cm. diameter. Previously a tonsillectomy had been done with little improvement. Microscopic confirmation of diagnosis. Treatment: 1000 mg.-hr. of radium, using 50 mg. with beta ray screen, at 1 inch distance. Prompt disappearance of swelling in six weeks. Clinically well three years later.

References

Molyneux, E. S. Radium as a curative agent for tuberculous glands. *Lancet*, 2: 804, 1922.

Molyneux, E. S. The treatment of tuberculous cervical adenitis by radium. *Brit. M. J.*, 2: 865, 1923.

Epithelioma of the Lip

Diagnosis is not discussed in this outline, but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Squamous-celled carcinoma of the lip comprises about 2 per cent of all carcinomata. The lower lip is attacked far more often than the upper, the vermilion border being the most common site. Flat squamous-celled lesions grow more rapidly and metastasize much earlier than the less malignant, more slowly growing, basal-celled varieties. Early crust formation on a slightly raised or indurated base, followed by alternate healing and crust formation or a rapid ulceration and extension of induration are the usual findings. Metastases may be early or late, depending upon the degree of malignancy and rapidity of growth. When both skin and mucous membrane are involved, the growth is ordinarily more rapid, metastasis occurs earlier and secondary growths are more often found in the deep lymphatic chains of the neck. Growth and extension may be delayed for months and years in the basal-celled type or may be rapidly fatal in a few months in the squamous-celled types.

Radium Indications. Radium is easily adapted to the treatment of epithelioma of the lip during all stages. The end results obtained by the use of radium in early lesions equal those of any other method. Its use is attended by less disability and deformity in the relatively early lesions and in advanced lesions its value is but little questioned. Radium applied interstitially or by the surface method with cross-fire or by means of deep external irradiation are all suitable for the destruction of local lesions. The draining lymphatics are easily reached with deep external irradiation. Clinical observation is simple. When there are no secondary growths, radium destroys the local lesion with a minimum of deformity. When secondary metastases are present in the neck, radium will accomplish satisfactory palliation. If surgical measures are instituted, radium serves well as a postoperative prophylactic measure.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. In general, three types of radium applications are made to carcinoma of the lip: the interstitial, the surface, and the deep external application.

The interstitial treatment employs radium element needles, with a screen allowing 10 to 15 per cent of the beta rays to pass. The dosage when employing the needles varies from 60 to 130 mg.-hr. per cubic centimeter of malignant tissue. Gold implants carrying from 1.0 to 2.0 mc. per seed are used to the extent of 1.0 to 2.0 mc. per cubic centimeter of malignant tissue. These applications are made under local anesthesia, removing the element needles at the required time, and allowing the radon implants to remain permanently in the tissues.

Surface applications are made by surrounding the lesion on all available sides with variously screened tubes, held in place by means of modelling compound or other mechanical means. The tubes may be held in direct contact with the lesion during the application or they may be raised from 0.5 to 1.0 cm. from the surface. From 50 to 100 mg.-hr. per square centimeter of surface usually suffices in surface applications. Surface application in smaller dosage may be used to supplement interstitial treatments. The surface method has the advantage of not puncturing the protective wall about the lesion and has the disadvantages of possible extensive mucous membrane and skin ulceration with its consequent delayed healing and its lack of economy in the use of radium. Some clinics employ the surface method exclusively.

Deep external irradiation may be employed to reinforce interstitial or surface applications and should be used in all cases to irradiate heavily the draining lymphatics. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance over the lymphatics of the neck probably gives the best promise of results. If metastatic nodules are present in the submental nodes or in the neck, the maximum skin dosage should be applied. One thousand to 1200 mg.-hr. with beta ray screen, at 1 inch distance, over each 2 sq. in. of skin surface, may serve as a standard.

Interstitial applications in the form of element needles or gold implants may well be used in extensive cervical masses. From 60 to 130 mg.-hr. per cubic centimeter of malignant tissues may be employed. Four to six weeks later block dissection of the cervical masses may be done. Radium in tubes, needles or radon in gold implants may be buried in the depth of the wound at the time of operation. In well-irradiated, selected cases, block dissection may be withheld awaiting evidence of regrowth. Both sides of the neck should be irradiated in all cases of epithelioma of the lower lip. Upper lip lesions are rare. Second applications may be made to local lesions six to eight weeks after the initial treatment should destruction be incomplete. Second applications encounter diminished blood supply, firmer fibrosed tissues and lowered local resistance to irradiation. Consequently dosage should be reduced from one-quarter to one-half. Deep irradiation may be repeated in six to eight weeks if the skin tolerated the initial dose well. A third or fourth application may be carefully made at intervals of two to three months in extensive and advanced cases, for the purpose of inhibiting the growth of the lesion, of attempting to heal ulcerations, and of promoting the patient's comfort.

Reaction. The general reaction is not marked in the average case of epithelioma of the lip except when a dose of several gram-hours is given over the neck within a short time. Malaise, headache, anorexia, nausea or vomiting may follow heavy external irradiation. Chiefly, the general reaction is secondary to the local changes.

When interstitial applications are made to early and moderately advanced lesions, there is a swelling of the lip for thirty-six to forty-eight hours due to instrumentation, and it then subsides. Between the fifth and the tenth day the reaction to the radium begins with swelling, occasional burning, and some pain. Frequently there occurs superficial ulceration of the skin or mucous membrane. The local lesion begins to shrink and slough within a few days after the local swelling reaches its maximum. This inflammatory reaction continues during the later second and third weeks, accompanied by disintegration of malignant cells and

liquefaction of cellular matter with resulting absorption or slough, so that by the fourth week repair is in progress.

When element needles are used, the reaction is of shorter duration than when radon implants are employed, since the implants deliver rays for a period of about thirty days.

By the fifth or sixth week healing and repair are complete in the favorable cases. When irradiation has been heavy or the growth extensive, the reaction may be prolonged or by the sixth or seventh week regrowth may be appearing.

When surface applications are employed, reaction with ulceration over the area treated begins in the second week. It is sometimes painful since the skin and mucous membrane undergo sloughing. The malignant cells undergo necrosis and absorption or slough during the second and third weeks. By the fourth week repair is in progress. Healing may be complete by the fifth or sixth week. Extensive lesions heavily irradiated may heal slowly, requiring six or eight weeks or more, and by that time recurrences or regrowth of undestroyed malignant tissue may appear.

Deep external irradiation with less than the erythema dose may give no visible reaction. Bronzing of the skin or epilation frequently results about the neck. Rarely do any complications arise. Infected growths may present a more extensive local inflammatory reaction with enlargement of neighboring lymph nodes, raising the question as to whether the enlargement of the glands is the result of metastatic growths or pyogenic infection. Conservatism should govern the physician in the handling of enlarged lymphatic glands of the neck when the local lesion is ulcerated or when they first appear during the reaction of the local lesion to irradiation. These nodes should be watched but not summarily condemned as malignant.

Favorable cases terminate with complete healing of the skin and mucous membrane, with a minimum of scarring, often none at all. Induration is not present, although thickening and lack of former pliability may result from the fibrosis. Hyperesthesias and paresthesias may be present about the irradiated area for some months. If the local lesion was extensive and irradiation has been adequate, a defect will be present where the lesion existed. If the de-

struction of the malignant cells has been incomplete, ulceration may persist and recurrence may appear as early as the sixth or the eighth week. It is occasionally possible to cause healing of extensive lesions, but these may later extend or recurrences may appear in adjacent parts, such as the mouth, the skin of the face, the neck, or even the upper lip, destroying completely the soft parts as the lesions advance. Secondary growths in the neck can in many cases be kept from breaking down to extensive ulceration and sinus formation if one carefully repeats the irradiation.

Prognosis. The prognosis is good in early localized lesions. Complete eradication without deformity is the rule in most of the cases. When secondary nodules are present, they constitute a serious problem. Usually the primary growth can be eradicated but the secondary growths in the neck are refractory. Block dissection preceded and followed by irradiation is practiced to advantage in some clinics. Deep external irradiation by radium supplemented by the burial of radium or radon in the depth of the wound at the time of operation or by the preoperative application of element needles or radon to the malignant masses, are thoroughly justifiable methods. When the cervical lymph nodes are the site of secondary growths, all means at our disposal should be combined to fight what is eventually too often a losing battle.

Case History

Mr. F. Aged fifty-eight. Epithelioma of lower lip. Ulcerated, encrusted, raised, indurated lesion of lower lip 1.5 cm. in diameter. Two palpable lymph nodes in cervical region. Treated with 225 mg. radium over involved nodes of neck with beta ray screen, totaling 4280 mg.-hr., at 1 inch distance over three areas. Also 62.5 mg. in needles to lip for six hours.

References

Aikens, W. H. B. The radium treatment of malignant disease of the lip and skin. *Canad. Pract. & Rev.*, 42: 142, 1917.

Angle, E. J., and Owen, L. J. Treatment of cancer of the lower lip with special reference to radium and electrocoagulation. *Urol. & Cutan. Rev.*, 27: 688, 1923.

Boggs, R. H. The treatment of epithelioma of the lower lip. *Interstate M. J.*, Suppl. Roentgenol., 2: 114, 1916.

Boggs, R. H. Radium and deep therapy in the treatment of malignancy (epithelioma or cancer of the lip). *Radium*, 18: 49, 1921–22.

Dubois-Roquebert. The radium treatment of carcinoma of the lips. *Paris méd.*, 12: 110, 1922.

Janeway, H. H. The treatmcnt of cancer of the lip by radium. *J. A. M. A.*, 70: 1051, 1918.

Kennedy, W. H. Epithelioma of the lip. *Radiology*, 4: 319, 1925.

Lain, E. S. A clinical study of epithelioma of the lower lip. *J. A. M. A.*, 75: 1052, 1920.

Lain, E. S. Treatment of cancer of the lip by radiation. *Arch. Dermat. & Syph.*, 6: 434, 1922.

Lammers, H. Radium treatment of cancer of the lip. *Acta Radiol.*, 2: 497, 1923–24.

McGuffin, W. H. Cancer of the lower lip. *Canad. M. A. J.*, 15: 1046, 1925.

Montgomery, D. W., and Culver, G. D. In reference to the behavior of radium in cancer of the lip. *Urol. & Cutan. Rev.*, 26: 16, 1922.

Montgomery, D. W. and Culver, G. D. Epithelioma of the lip treated with radium. *California & West. Med.*, 22: 628, 1924.

Norsworthy, O. L. Treatment of cancer of the lower lip. *Texas State J. Med.*, 20: 184, 1924.

Pfahler, G. E. Cancer of the lip treated by electrocoagulation and radiation. *Arch. Dermat. & Syph.*, 6: 428, 1922.

Pinch, A. E. H. Epithelioma of the lip. A report of the Work at the Radium Institute, London, Jan. 1, to Dec. 31, 1922. *Radium*, N. S., 2: 46, 1923.

Quick, D. Radium in the treatment of epithelioma of the lip. *J. Radiol.*, 2: 1, 1921.

Stevens, J. T. Cancer of the lip. *Radiology*, 4: 372, 1925.

Wall, C. K. Cancer of the lip. *J. M. A. Georgia*, 12: 67, 1923.

Wilkins, H. F., and Gewin, W. C. The treatment of cancer of the lip with radium. *Urol. & Cutan. Rev.*, 26: 46, 1922.

Lymphosarcoma

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The term should be restricted to local sarcomatous growths in single nodes, infiltrating beyond the capsule and composed of distinct types of cells, such as round or the spindle cells, or multiple types growing simultaneously. The types of cells may vary considerably in proportion to the vascular changes. If vascular changes are marked, the lesion may be angiomatous; if the endothelial changes are marked, the lesion is more likely to be endotheliomatous. Lymphosarcomata are highly malignant, infiltrating lesions, markedly cellular, rapid of growth and running a short, clinical course if untreated. The cervical,

axillary, and mediastinal glands are most frequently involved. It is probable that most mediastinal tumors are lympho-sarcomatous.

Radium Indications. Radium therapy is well adapted for the destruction of markedly cellular, rapidly proliferating sarcomata. This type of cell seems to be especially susceptible to radium rays. The application is usually simple and the danger slight; there are few real contraindications except the danger of temporarily increasing pressure on vital organs by the primary swelling of the sarcomatous mass which appears at once after irradiation and lasts for several days.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external gamma ray treatment is the usual method. From 1000 to 1200 mg.-hr. at 1 inch distance over each 2 sq. in. of skin surface, employing the gamma ray only, may serve as fair standard and should be applied from all directions possible for cross-fire technic. Intense irradiation with an applicator containing from 1 to 4 gm. at 6, 10 or 15 cm. distance, probably gives the best promise of success. Interstitial treatment, when possible, is advisable. Element needles giving 75 to 100 mg.-hr. per needle, using 12 per cent of the beta rays, or gold implants of radon in dosage of 1.0 to 2.0 mc. per cubic centimeter constitute appropriate treatment by this method. In planning radium therapy, either by the interstitial or the deep external method, the tissues one to two centimeters beyond the clinical borders of the lesion should be heavily irradiated, especially in the direction of the draining lymphatics. Applications may be repeated in eight to ten weeks if the skin will tolerate it. Interstitial treatment may be repeated in eight to ten weeks, but one should reduce the dosage on account of fibrosis and reduced vascular supply due to the previous treatment. Missed areas, prompt recurrences or extension may be treated in four weeks if the skin reaction permits. Re-treatment may be applied advisedly after intervals of two or three months if required to control the growth.

Reaction. The general reaction is often severe in extensive lesions. When 5 or 10 gm.-hr. or more are given within a few days, malaise, anorexia, headache, nausea, and occasional vomiting with slight fever may begin during the application. These symptoms continue in many cases for two or three weeks, depending upon the extent and rapidity of cellular destruction. Intoxication from the absorption of the cellular debris from the tumor increases the general reaction. A mild degree of anemia may be produced. The reaction usually subsides by the fourth or fifth week. Convalescence progresses rapidly unless the case is too far advanced. Locally, the reaction begins in a few days when the external method is used and is characterized by a diffuse swelling and increased pressure which are quickly followed by marked decrease in the size of the mass. The susceptibility of the individual lesion treated is often indicated by the rapidity with which the tumor shrinks and disappears. The interstitial method yields more prompt reaction with perhaps greater preliminary swelling and more intense and prolonged reaction from the absorption of toxic material, especially if radon implants are employed. Unfortunately, recurrence due to insufficient or faulty irradiation is likely to occur as promptly as did the decrease in size following the initial treatment. Recurrences or extensions appear most commonly from the recesses of the tumors which have been treated with insufficient deep external irradiation or in adjacent, untreated lymphatic tissues. Favorable cases yield promptly within a month and remain quiescent for a variable number of months, rarely years. Unfavorable cases grow again promptly and progress rapidly to the patient's death within a few months.

Prognosis. Lymphosarcomata in many instances yield very readily and satisfactorily to radium treatment, but unfortunately recurrences or regrowths are as prompt and as disappointing as the earlier changes were gratifying. Few cases yield for a very long time. Cures are not at all common, but radium treatment is well worth while at least for its palliative effect, and occasionally one is rewarded by a long deferred recurrence and at rare intervals an apparent cure.

Case History

Mr. L. Aged twenty-three. Lymphosarcoma (biopsy). Glands of neck removed on clinical diagnosis of tuberculous glands. Microscope revealed lymphosarcoma. Nodules 1.0 to 2.0 cm. in diameter recurred in three months in cervical and supraclavicular areas. Treated by 7200 mg.-hr., using 100 mg. radium at 1 inch distance, with beta ray screen over the involved glands, in three sittings at intervals of one week. Nodules reduced three-quarters in size, and remained quiescent one year. Clinically well two years.

References

Bissell, J. B. Radium treatment of lymphosarcoma of neck and face. *Internat. J. Surg.*, 31: 112, 1918.

Desjardins, A. U. Radiotherapy for lymphoblastoma. *Radiology*, 7: 121, 1926.

Kelly, H. A., and Burnam, C. F. Radium demonstration at the Howard A. Kelly Hospital. *South. Surg. & Gyn. Assn.*, 31: 193, 1918.

Minot, G. R. Lymphoblastoma. *Radiology*, 7: 119, 1926.

Carcinoma of the Floor of the Mouth, Cheek and Alveolar Process

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The lesion, which is squamous-celled in type, and usually rapidly growing, is fungating more often than eroding, bleeds easily, gives little pain early, spreads by extension, and metastasizes to the submaxillary and deep cervical glands rather early. These growths are closely associated with a foul acid condition of the mouth, jagged teeth, tobacco, and lues. Syphilitic and malignant ulcerations often coexist.

Radium Indications. Radium therapy is preeminently indicated. Interstitial applications offer better hope of local lesion destruction without recurrence, than the knife, cautery, or electric heat. When large fungating masses are present, mechanical removal of the redundant portions with adequate irradiation of the base may well be employed. The beta rays are chiefly used in causing necrosis of all malignant cells with a minimum of damage to normal structures.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Lesions of the buccal mucous membrane, including the floor of the mouth, the alveolar process and the

cheek, are best treated by interstitial applications of radon or by element needles of various sizes and strengths. Reenforcement or cross-fire from gamma or deep irradiations applied over the adjacent skin is necessary. The lymphatics draining the site of the lesion should be irradiated heavily. One thousand milligram-hours from 50 mg. units at 1 inch distance serve as a standard dosage which may be varied with the amount of radium available. One thousand milligram-hours per 2 sq. in. of skin surface is usually well tolerated. Surface applications seem to have become less popular because of the unnecessary reactions and ulcerations of normal mucous membrane and consequent distress. Exception to this rule might be made when the lesion, lying close to bone, is less than 5 mm. in thickness, in which case heavily screened radium might be laid against the lesion, hoping thereby to destroy malignant cells only and to preserve a tissue framework as a covering for the bone. Mouth washes and other attempts at mouth sanitation should precede the application. Implants or needles should be inserted from without the area of the ulceration, but if this is impossible, then injection must be made directly through the ulcer. In the use of glass implants it is more important that they be lodged within the indurated area than when needles are employed for with the latter there is less necrosis of normal tissue, only the more penetrating beta rays escaping from the needles. Gold implants of 1.0 to 2.0 mc. or glass implants of about 0.5 mc. each should be lodged homogeneously throughout the lesion, taking care to place none within 0.5 cm. of bone. If it is impossible to realize this latter precaution, the size of the implants should be reduced to prevent bone necrosis. Standard steel needles of suitable size may be used, irradiating each cubic centimeter of tissue to the extent of 60 to 90 mg.-hr. Needles and implants should be kept more than 0.5 cm. from the skin of the cheek to prevent, if possible, perforation. Gamma irradiation from without will usually take care of malignant cells close to the skin, and there is much less danger of perforation or dimpling.

Lymphatics directly draining the lesion should be irradiated to the extent of 1000 mg.-hr., with 50 mg. and a beta ray screen, at 1 inch distance, according to the amount of

radium available. Intense irradiation over the lymphatics of the neck with an applicator containing from 1 to 4 gm. of radium, at 6, 10, or 15 cm. distance, probably gives the best promise of results. It is believed that such external irradiation, preceding the interstitial application, tends to prevent dissemination, to a certain extent sealing the lymphatics. Second applications may be made six to ten weeks later, in case of failure to destroy the local lesion entirely. Glandular metastases, persisting after adequate initial irradiation, may be treated again in six to eight weeks, or surgical excision and irradiation may be considered. Gentle mouth sanitation should follow the applications but no vigorous attempts should be made to separate sloughs or hasten the reaction. Rarely secondary hemorrhage occurs. If perforations of the cheek occur and the case, in six months or so, gives promise of clinical cure, plastic surgery is indicated. Repeated external or even interstitial applications should not be withheld from incurable cases if the general health is fair. Palliation in these cases is well worth trying for. Each succeeding application is rendered more difficult by reduced blood supply and increased fibrosis, thus increasing the danger of slough *en masse*. Even in extensive and advanced cases, palliative treatment is indicated, for death by toxemia is preferable to one by starvation with hideous, foul, sloughing deformities.

Reaction. The general reaction is relatively mild, unless several gram-hours are given externally. Malaise and anorexia ordinarily occur with only occasional nausea. The patient is ambulatory throughout the three to five weeks of general reaction.

Local reaction begins almost with the application and reaches its height during the third week or a little later, when implants are used. It persists four to five weeks in the needle cases and as much as eight weeks in the case of the implants. Inflammatory swelling with disintegration and sloughing or absorption begin eight to ten days after application, and the healing and fibrosis are completed from the twentieth to the fortieth day. Pain is present in all cases to a varying degree, more severe and of longer duration by the implant method. Mild sedatives, mouth washes, and the free use of fluids greatly reduce the local and

general reactions. The end result, if the treatment is successful, is a smooth mucous membrane, slightly scarred, dimpled or puckered. There is a sort of rubbery sensation on palpation; often it is difficult to distinguish between this rubbery fibrosis and the induration of incomplete destruction or recurrence.

Prognosis. The prognosis is ultimately grave in cases presented for treatment in any but the earliest stages. Local destruction can often be accomplished but the areolar nature of the floor of the mouth does not promote healing readily if the irradiation causes extensive necrosis. In alveolar lesions, tissue for regeneration is often lacking; and, where bone is exposed, osteomyelitis or extension into the bone are to be feared. Cheek lesions do better. Metastases, when present, must be vigorously and repeatedly irradiated or resort must be had to surgical excision with preoperative and postoperative irradiation. Irradiation should not be withheld, even from the advanced cases, if the general health is fair. External irradiation alone prevents revolting terminal pictures, and the final sufferings are greatly mitigated.

Case History

Mr. W. Aged forty-nine. Ulcerated, indurated, friable, bleeding lesion, 1.5 cm. in diameter, located on dorsum of tongue. Pathologist's diagnosis: squamous-celled carcinoma; no palpable glands of the neck. Treated by 100 mg. radium in form of 8 needles (12 per cent beta rays) in and about lesion for eight hours, totaling 800 mg.-hr. Also 1700 mg.-hr., with beta ray screen, over lymphatics of neck at 1 inch distance, using 100 mg. radium for seventeen hours. Clinically well six years.

References

Boggs, R. H. Radium treatment of mouth and throat. *Penn. M. J.*, 25: 22, 1921.

Brewer, G. E. Carcinoma of the lip and cheek. *Surg., Gynec. & Obst.*, 36: 183, 1923.

Dickinson, B. M. Malignant disease of the throat. *Penn. M. J.*, 21: 612, 1918.

Field, C. E. Radium therapy of cancer of the mouth and throat. *New York State J. Med.*, 22: 121, 1922.

Gilbert, R. Ulcerative spindle cell cancer of the cheek treated by radium and roentgen rays. *Bull. et mém. Soc. radiol. méd. de France*, 11: 248, 1923.

Greenough, R. B. Radium in the treatment of carcinoma of the buccal cavity. *Boston M. & S. J.*, 178: 598, 1918.

Grier, G. W. The treatment of intra-oral carcinoma by contact application of radium. *Am. J. Roentgenol.*, 15: 201, 1926.

Johnson, F. M. Certain difficult problems in the treatment of carcinoma of the lower jaw. *Radiology*, 5: 280, 1925.

Jones, A. C. Report of radium cases of head and neck. *Northwest Med.*, 21: 140, 1922.

Lenz, M. Curie therapy of epidermoid carcinoma of the intra-oral group as carried out at the radium institute, Paris. *Am. J. Roentgenol.*, 15: 210, 1926.

New, G. B. The use of heat and radium in the treatment of cancer of the jaws and cheeks. *Radium*, 14: 9, 1919–20.

Pinch, A. E. H. Epithelioma of the cheek. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 62, 1923. *Radium*, N. S., 2: 47, 1923.

Pinch, A. E. H. The salivary glands. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922.

Pollock, H. L. Primary and metastatic cancer of the head. *J. Michigan M. Soc.*, 25: 131, 1926.

Pfahler, G. E. The treatment of malignant disease about the mouth by combined methods. *J. A. M. A.*, 67: 1502, 1916.

Quick, D. Radium in intra-oral cancer. *Urol. & Cutan. Rev.*, 27: 219, 1923.

Quick, D. Carcinoma of the floor of the mouth. *Am. J. Roentgenol.*, 10: 461, 1923.

Ruggles, E. W. An efficient method of applying radium within the mouth. *J. A. M. A.*, 80: 1374, 1923.

Simmons, C. C. Cancer of the mouth. *Surg., Gynec. & Obst.*, 43: 377, 1926.

Simpson, F. E., and Flesher, R. E. Radium emanation in treatment of intra-oral cancer; with report of 141 cases. *Tr. Sect. Dermat. & Syphilol., A. M. A.*, pp. 120–129, 1925.

Simpson, F. E., and Flesher, R. E. Radon therapy (radium emanation) as palliative agent in treatment of intra-oral cancer. *J. A. M. A.*, 87: 655, *J. Cancer*, 3: 18, 1926.

Simpson, F. E., and Flesher, R. E. Radon (radium emanation) in treatment of intra-oral cancer. *Illinois M. J.*, 50: 305, 1926.

Parotid Tumors

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Under parotid tumors may be included a heterogeneous group of neoplasms varying greatly in gross and microscopic structure, with varying degrees of malignancy and susceptibility to dissemination. The malignancy of such tumors is usually not of high degree. Either epithelial or endothelial origin is possible, though the latter is unlikely. Grossly, the neoplasm may be soft and fluctuant,

firm, hard, lobulated, diffuse, or circumscribed. The cellular structure may be carcinomatous, mixed-celled, or sarcomatous. The term "mixed-celled tumor of the parotid" might describe briefly most of these tumors. Usually they are of slow growth, metastasize rarely, and grow by extension to adjacent structures. Long periods of quiescence are not uncommon. Surgical excision is frequently accompanied by a recurrence which is clinically of much greater malignancy, especially if the primary tumor was not encapsulated.

Radium Indications. The accessibility of these tumors for treatment and observation, together with the susceptibility of mixed-celled tumors to radium rays, renders radium an extremely valuable agent in dealing with parotid growths. Surgical intervention not infrequently seems to change a benign growth into a malignant neoplasm. So radium is attended with less risk of stimulation and dissemination. When complete or partial surgical excision has been performed, postoperative irradiation to the skin tolerance dose is strongly indicated to prevent or delay local recurrence.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Deep external irradiation and interstitial methods are available for the treatment of parotid tumors. Deep external treatment to the extent of 1000 to 1200 mg.-hr. of gamma radiation at 1 inch distance over each 2 sq. in. of surface is a standard of dosage to be applied. The whole glandular area together with 1 or 2 inches beyond the clinical margin should be irradiated. A total dosage of from 4 to 10 gm.-hr. may be given, according to the amount of radium available and the distance employed. Intense irradiation with an applicator containing from 1 to 4 gm. of radium, at 6, 10 or 15 cm. distance probably gives the best promise of success. Interstitial irradiation by means of element needles or radon implants may be used. From 100 to 130 mg.-hr. or mc.-hr., employing 10 to 15 per cent of the beta rays, may be given per cubic centimeter of tumor tissue. One may use gold implants containing from 1.0 to 2.0 mc. for each cubic centimeter of tissue. The tissues 1 to 2 cm. beyond the clinical margin of the growth should be

included in the treatment. If complete interstitial irradiation of the tumor is uncertain or impossible, supplementary deep external irradiation should be given at the same time, perhaps slightly reducing the interstitial dosage to prevent extensive sloughing. In general it may be said that external therapy is safe and often effective without fear of traumatic dissemination which may be produced by interstitial insertion. Applications may be repeated in six to ten weeks, bearing in mind the skin reaction at the initial treatment and the increased fibrosis and decreased vascular supply. The dosage with second interstitial applications should be reduced 50 per cent in areas treated previously. Missed areas, extensions, or recurrences should be irradiated in the same manner as the primary growth, boldly facing the possibility of sloughing, in view of the seriousness of the recurrence or extension. Recurrence of growth or extension indicates re-treatment, according to the rapidity with which the extension or recurrence appears and according to the degree of success attending the initial treatment.

Reaction. The general reaction may be mild or marked, depending upon the dosage and the character and size of the tumor. With dosage of 6 to 10 or more gram-hours in susceptible tumors, the general reaction may be characterized by malaise, anorexia, vomiting, headache, and weakness. Locally, the swelling and pain may be marked. The reaction begins while the heavy irradiation is being given and continues for three or four weeks, being more intense during the irradiation and again during the second and third weeks. With external irradiation the local inflammatory reaction appears from five to ten days after treatment. Swelling of the tumor and adjacent parts with subsequent shrinkage and finally increased firmness and fibrosis succeed one another during the four or five weeks of clinical local reaction. Cell disintegration by autolytic degeneration, absorption and fibrous tissue replacement and contraction constitute the cellular reaction in the case of a susceptible tumor. Interstitial treatment results in an earlier reaction by a few days, with complete caustic necrosis about the implants or needles and autolytic degeneration at a greater distance. In the case of radon implants, the reaction continues for a longer period,

inasmuch as the rays are being delivered during many days instead of for one day, as is the case when element needles are used. The reaction has usually subsided by the sixth week at which time clinical observations reveal the results of treatment as regards shrinkage, missed or under-irradiated areas, and even the presence of recurrences and extension. Pain, due to swelling and inflammatory reactions, may be severe during the height of the reaction. Involvement of the facial nerve in the irradiated area may give rise to referred pain, or subsequent contraction about the nerve may cause pain. Favorable cases shrink to a fibrous remnant, quiescent for varying periods of time. Unfavorable cases show but little reduction in the size of the tumor, and that only temporarily. Extension and recurrence are not uncommon. In favorable cases the lesion remains stationary for months or years.

Prognosis. A fair proportion of parotid tumors yield promptly and completely to adequate radium treatment. This treatment is probably safer and is attended with better results than any other. Postoperative irradiation tends to delay and inhibit recurrence.

Case History

Mrs. G. Aged thirty-three. Mixed tumor of parotid. Postoperative irradiation along line of incision. Treated by 4250 mg.-hr. of radium at 1 inch distance, beta ray screen, using 100 mg. radium over four areas. No recurrence, one year.

Reference

Quick, D. A. and F. M. Johnson. Radium treatment of parotid tumors. *New York State J. Med.*, 22: 297, 1922.

Epithelioma of Penis and Anus

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Squamous-celled carcinoma of the penis or anus differs from that found elsewhere, chiefly because of the difference in anatomic structure of these organs and their immediate surroundings. Epithelioma of the penis develops most often on the prepuce, grows rapidly, fungates, perforates the prepuce or glans early, and frequently

metastasizes to the inguinal glands. Epithelioma of the anus is superficial at first, and spreads rapidly to involve the glabrous skin or mucous membrane. When both skin and mucous membrane are involved, the rate of growth is increased. The subcutaneous areolar tissue offers little resistance when infiltration extends into it. Trauma from friction and from constant moisture and irritation from defecation or urination contributes to the spread of epidermoid carcinoma of the anus and penis.

Radium Indications. Radium is well adapted for the destruction of malignant growths developing on the anus and penis. These organs are of easy access for application and observation. Early lesions will yield and heal. When both skin and mucous membrane are involved and the induration is 3.0 mm. or more thick, deep rays must be employed to produce destruction of the deeper lying cells by autolysis rather than by the caustic action of the beta rays. When the subcutaneous structures about the anus and the mucous membrane about the sphincter ani are involved, surface and deep external irradiation in liberal amounts are required to eradicate the disease. If the glans penis and prepuce are involved, erosion of the corpus cavernosum soon follows, and heroic surface applications are required if destruction of the malignancy is to be accomplished. When metastases are present in the groin or in the space of Retzius, deep external irradiation to the limit of skin tolerance is required to inhibit the spread of the malignancy. Extensive local pyogenic infection contraindicates radium treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. In general, both superficial and deep irradiations are employed in lesions of the penis and anus. The caustic action of the soft beta rays on the subsurface tissues in these locations seems to leave little power of repair. The caustic action of radium tends to encourage hemorrhage from the corpus cavernosum in penile lesions. The soft areolar tissues about the anus offer little resistance to either the radium rays or the disease, and sloughs are

common, leaving almost an unhealable defect. Full strength glazed plaques, screened with metal up to 0.5 mm. of lead to absorb the soft beta rays, may be applied for from two to six hours in indurations 2.0 to 3.0 mm. in thickness. Superficial lesions less than 2.0 mm. in thickness may be destroyed with unscreened full strength plaques, with exposures of from one to two and one-half hours. When the induration is more than 3.0 mm. thick, only the hard beta and gamma rays should be employed.The cells in the depth of the lesion must be destroyed but it is better to accomplish this by the slower autolytic disintegration than by the caustic action. Intense irradiation with an applicator containing from 1 to 4 gm. of radium, at 6, 10 or 15 cm. distance, applied over the lymphatics draining the area involved, especially the groin, probably offers the best hope of success. Slow disintegration and autolysis permits vascular regeneration and the gradual laying-down of fibrous tissue. Second applications may be made four to six weeks after the first, to attack undestroyed malignant tissue or to treat early recurrences. Subsequent applications may be made to belated recurrences or to inhibit the progress of refractory lesions.

Reaction. The general reaction to radium treatment of epithelioma of the anus or penis is mild or absent.

Locally the reaction is often severe and painful, due to the frequent irritation of micturition or defecation. The inflammatory reaction begins from the seventh to the tenth day with redness, swelling and pain. By the third week the disintegration and surface sloughing will be in progress. Shrinking of the indurated mass will be complete by the fourth week and repair follows rapidly in successful cases. Healing is complete usually by the fifth week. When destruction of the malignant cells is complete, healing will occur, but if ulceration persists, recurrence should be watched for carefully. Regrowth may be evident by the fifth or sixth week. During the period of painful inflammatory reaction, anodynes or even opiates may be required. Cleanliness of the parts should be secured by irrigations with boric acid, potassium permanganate or hydrogen peroxide solutions. The parts should be covered lightly

with wet boric acid packs, to be changed after urination or defecation. Rectal suppositories containing opium may be required if the anal sphincter is involved in the inflammatory reaction. Rarely will swelling occlude the urethra though urination may be extremely painful. In anal lesions where the sphincter is involved in the lesion or reaction, healing may be delayed five or six weeks. In successful cases, a smooth, slightly depressed, fully healed scar will result. In unsuccessful cases, indurated tissue may persist and the malignant process begin to reinvade as early as the sixth week. Before attempting subsequent irradiation one must decide whether he will seek complete eradication or be satisfied with palliation only. When neighboring lymph nodes are involved, it seems advisable to attempt palliative treatment only. Efforts should be made to eradicate the primary lesion if possible. In advanced or deep-seated lesions, or when secondary growths are found, palliative treatments only should be attempted, carefully weighing the severe reaction against the discomfort and clinical course of the lesion if left untreated.

Prognosis. Early superficial lesions, not invading both skin and mucous membrane, yield well to radium treatment. When the lesion has infiltrated the subcutaneous tissues about the anus or the sphincter, or the corpus cavernosum in the penis, only the most heroic treatment and favorable reaction and repair will accomplish eradication of the disease. When erosion of the glans penis has occurred, secondary growth in the draining lymph nodes has already occurred as a rule, and palliation is about all that can be hoped for. In anal lesions when ulceration has extended into the perirectal tissues, or when both sides of the sphincter are involved, only palliative treatment is justified.

Case History

Mr. C. Aged fifty-two. Epithelioma of anus. Ulcerating, fungating growth, 4.0 by 1.5 cm., extending anteriorly from anus. Induration involves lumen of bowel for 3.0 cm. In four months patient received 15,000 mg.-hr., 1200 of which were in form of interstitial needling; altogether sixteen applications. There was marked local and general improvement with gain of 20 pounds in weight and relief of pain. Eventual demise from the disease, one and one-half years later.

References

Dean, A. L., Jr. The treatment of epithelioma of the penis with radium and roentgen rays. *Am. J. Roentgenol.*, 15: 36, 1926.

Dean, A. L., Jr. Four cases of epithelioma of the penis treated by radium. *Med. J. & Rec.* (Suppl.) 119: 115, 1924.

Carcinoma of the Rectum

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. This lesion in the rectum is commonly of the adenomatous type, usually characterized by columnar cells. Occasionally it is scirrhous and of slower growth and extension. Squamous-celled lesions rarely develop about the anus and mucocutaneous junction. When present, they extend both into the rectum and out upon the adjacent skin. Adenocarcinoma of the rectum involves the wall linealy and annularly, infiltrating deeply and often projecting fungating masses into the lumen. Local ulceration and bleeding are common. Foul mucous discharge appears early, and there is painful defecation with stools smeared with bright red blood. A vain impulse to defecate is often the earliest symptom. Annular and projecting growths stenose. There is often noted early constipation, later alternating with diarrhea. Metastases to the liver or neighboring lymph nodes appear early in fungating, rapidly growing lesions. Annular scirrhous growths frequently give symptoms arousing suspicion long before secondary extensions are present. The common site is within digital range, but occasionally only proctoscopic examination reveals the lesion.

Radium Indications. Radium in various forms is well suited to destroy or inhibit this common malignancy. Either the caustic action of element needles or the more slowly necrosing action of the gamma rays are available for use in these lesions. Both may be combined in certain cases. The lesions are ordinarily readily accessible for application and subsequent observation. The resistance of adjacent normal bowel and the remoteness of vital structures permit adequate dosage with little fear of dangerous complications or sequelae. When a colostomy has relieved the rectum from

functioning, conditions are favorable for efficient radium therapy.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The applicator in most common use is the capsule inserted within the lumen of the involved segment, carrying a beta ray screen and encircled with rubber as thickly as the canal permits. Such applicators are best suited for annular lesions. Unilateral or hemispheric lesions require unilateral or hemispheric packing or "building up" with rubber to increase the distance between the radium and the normal mucosa of the uninvolved segment. Eccentric leaden applicators with the thin side turned toward the lesion are practical. The greater distance obtained by packing or building up reduces the irradiation to the normal mucosa quite as much as heavy leaden applicators of 3.0 or 4.0 mm. thickness and is preferred because it insures closer apposition of the radium to the surface of the lesion. The length of the capsule may be adjusted to the length of the lesion or a shorter capsule may be moved from segment to segment to insure the proper distribution of homogeneous radiation to all parts. Often the capsule is inserted with the examining finger as a guide. If this method is impractical, the insertion is made with the aid of the proctoscope or by careful sounding and mensuration. If stenosis is present, the caliber of the applicator is reduced by using less rubber or by employing gold or platinum screens. The shaft of the applicator must be semirigid and be firmly anchored against the anus by a lug or other suitable mechanism. Lead shafts bent sharply against the sacrum and fixed are satisfactory in some instances. Suitable dosage varies from 1000 to 1200 mg.-hr. per 2 inch segment, larger doses being tolerated in annular lesions and in cases where a colostomy has been done. Subsequent applications may be made in six to eight weeks if incomplete destruction has followed the initial application. When a colostomy has been done, a through and through cord may be used to carry the radium capsule to the proper segment, controlling the application by careful mensuration or by the fluoroscope.

Deep external irradiation from the sacral, pubic and perineal surfaces may well supplement the cavity application. Intense irradiation with an applicator, containing from 1 to 4 gm. of radium, may be applied over the lesion at 6, 10 or 15 cm. distance, from the skin using many portals of entry. Such treatment probably offers the best hope of success. In annular and scirrhous lesions, cavity applications serve best. When the lesion is fungating, linear or projecting markedly into the lumen, some form of interstitial application is often advisable. Gold implants containing from 1.0 to 2.0 mc. of radon are inserted into the base of the growth when it can be well outlined. A standard dose is 1.0 to 2.0 mc. per cubic centimeter of tissue. Element needles, employing 10 to 15 per cent of beta rays, may be inserted into the mass, delivering from 80 to 130 mg.-hr. per cubic centimeter of tissue. In making interstitial applications one should remember that a distance of about 0.5 cm. is necessary between the outer bowel wall and the implanted radium. The caustic action of the radium may erode the bowel wall, causing perforation or hemorrhage into the perirectal tissues. Large fungating masses may be destroyed by actual cautery or by electrocoagulation and the base later irradiated with gamma ray surface applicators. A colostomy undoubtedly greatly improves the results of radium therapy and should be urged as a preliminary procedure in all cases of carcinoma of the rectum. In some European clinics radium needles of 0.5 mm. of platinum wall thickness are inserted into the growth after complete mobilization of the rectum. These needles contain 1.33 mg. of radium element to each 15 mm. of length. Such needles are left in place from five to seven days.

Squamous-celled carcinoma arising about the anus presents a more complicated problem than lesions within the sphincter. Surface applications to this area are more distressing to the patient and require more ingenuity to secure homogeneous distribution of the radiation than do the internal lesions.

When the skin is involved, applications to the surface to be successful must be heavy. Interstitial applications are rendered more difficult on account of the loose avascular

nature of the subcutaneous tissues about the anus. Malignant subcutaneous invasion at this site is intractable. Caustic destruction about this area leads to deep craters which heal with great difficulty, if ever. Gold implants only should be used interstitially. Surface application alone is often inadequate for the arrest of the disease. In well-developed lesions about the anus, a colostomy is essential if anything but palliation is to be attempted with radium. Surface applications, employing 10 to 15 per cent of the beta rays homogeneously over these lesions, serve best. A proper dosage consists of 50 to 90 mg.-hr. per square centimeter with this screening. It may be repeated in six to eight weeks if indicated.

Prophylactic irradiation after radical excision in operable cases may well be employed. Eight hundred to 1200 mg.-hr. per 2 inch segment of operative field may be given, gaining access through an aperture in the perineal or sacral wound left for the purpose. Radiation may be used as soon after the operation as the patient's general condition permits. Free open drainage is advisable for two to three weeks.

Reaction. The general reaction from rectal irradiation is usually not severe, consisting for the most part in general depression and malaise. If a colostomy has been done, the reaction is mild, probably because of freedom from the irritation of fecal matter passing over the acutely inflamed segment. Heavy external irradiation increases the general reaction in proportion to the amount given. Nausea and vomiting may then also be present. The reaction comes on primarily at the time of irradiation and lasts intermittently for four or five weeks, increasing markedly during the third week if there is much tissue destruction and toxic absorption.

Locally the reaction is that of inflammation, with ulceration and sloughing most marked in the third week. If the segment must function, local pain and distress are increased, especially by defecation. Bloody mucous discharge is present at first, with gradual decrease in the amount of blood and increase in mucus, and sometimes fragments of slough. By the fourth week, as a rule, the discharge is becoming less, and has practically disappeared by the sixth if destruction is complete. Stenosis from annular contraction of

scar tissue is an unfortunate complication in about 10 per cent of the annular lesions. Satisfactory end results present a smooth, pale mucosa, scarred, perhaps adherent, and a moderate distortion of the bowel, but, barring marked annular contraction, the segment is not much impaired as to function. Local measures for relief are best restricted to analgesic or quieting suppositories. Local applications and trauma are to be avoided. Mineral oil in liberal amounts reduces fecal traumatism. General supportive measures, such as increased fluids, iron and bitter tonics, forced nourishment and rest with stimulants are advisable here as in other instances of heavy irradiation.

Prognosis. The results are often encouraging. Complete arrest for months is not uncommon, even in inoperable cases. Freedom from symptoms, local or general, may be hoped for in any but the advanced cases. Because of the superior results from radium when used in conjunction with colostomy, there is little doubt that this surgical procedure is amply justified. Months of relative comfort may be obtained in a large proportion of cases until intractable recurrence or secondary lesions appearing in the liver or elsewhere indicate the beginning of the end. Squamous-celled lesions about the anus are intractable, but even here radium offers the best palliation.

Case History

Mrs. U. Aged thirty-three. Carcinoma of rectum. Pain in the rectum following excision of tumor mass in anterior rectal wall with microscopic diagnosis of carcinoma. Recurrence prompt. Treated with 3000 mg.-hr. radium, using 100 mg., part in rectum and part in vagina. Three sittings in three weeks time. Beta ray screen. Clinically well after eight years.

References

Bower, J. O. Operating cystoscope in application of radium to cancer of the rectum following colostomy. *Surg., Gynec. & Obst.*, 34: 539, 1922.

Bowing, H. H. and Anderson, F. W. The treatment by radiation of cancer of the rectum. *Am. J. Roentgenol*, 10: 230, 1923.

Bowing, H. H. Significant cellular changes observed in irradiated tissue, especially of cancer of the rectum. *Radiology*, 4: 378, 1925.

Coffey, R. C. Treatment of cancer of the rectum. *Ann. Surg.*, 76: 500, 1922.

Crile, G, W. Treatment of carcinoma of colon. *Ohio State M. J.*, 119: 5, 1923.

Gaarenstroom, G. F. Combined radiotherapy of rectal cancer. *Nederl. Tjdschr. v. Geneesk.*, 66: 2165, 1922.

JONES, T. E. Radiation treatment of cancer of the rectum. *Radiology*, 5: 306, 1925.

DE LABORIE, B. and LORY. Technic for applying radium in low tumor of the rectum. *J. de radiol. et d'electrol.*, 7: 493, 1923.

LABORIE. Technic for applying radium in low tumor of the rectum. *J. de radiol. et d' électrol.*, 7: 493, 1923.

NEUMAN. Technic and immediate results of curiepuncture and methods of approach in cancer of the rectum. *J. de radiol. et d'électrol.*, 7: 548, 1923.

PELLIZZARI, C. Radium treatment of carcinoma of the rectum. *Riforma med.*, 131: 309, 1915.

PINCH, A. E. H. Carcinoma of the rectum. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 59, 1923.

PROUST, R. Retrorectal application of radium in cancer of the rectum. *Bull. et mém. Soc. de chir. de Paris*, 47: 1204, 1921.

QUICK, D. The treatment of cancer of the rectum by radium. *Am. J. Roentgenol.*, 8: 746, 1921.

TOUSEY, S. Pericecal tumor. *Med. Rec.*, 101: 356, 1922.

SARCOMA OF THE SOFT PARTS

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. Sarcomata of soft parts are multicellular, vascular, unencapsulated tumors, into which hemorrhage is common. Metastasis takes place more often by the blood stream than by the lymphatics; however, free cells may break off and travel by way of the lymphatics as well. The degree of malignancy depends on the extent of the reversion to embryonic type; the greater the reversion, the greater the degree of malignancy. These tumors are made up of several varieties of cells, including small round, large round, small spindle, large spindle, oat shaped, and mixed cells. Those containing one type of cell are pure sarcoma. Depending upon the type of tissue intermingled with the cells, they may also be called fibrosarcoma, osteosarcoma, chondrosarcoma. Ordinarily malignancy is of high degree and the growth rapid.

RADIUM INDICATIONS. Radium rays are capable of causing complete necrosis by their caustic action and by autolysis. Rapidly growing tumors, with markedly undifferentiated cells, are extremely susceptible to radium rays.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The interstitial method offers the best results. Radium element needles or radon implants may be inserted into the mass. Deep external irradiation is sometimes the only method advisable. The choice of method depends upon the location of the tumor, the mechanics involved in the interstitial method, and the proximity of the growth to vital structures. When the tumor invades vital organs the method of application depends upon the object in view in the treatment. If an attempt to cure is to be made, the interstitial method should be employed. If palliation only is the object than deep external irradiation is the method of choice. Surface application is occasionally advisable. When the interstitial method is employed, 1.0 to 2.0 mc. gold implants are inserted, one for each cubic centimeter of malignant tissue, being sure to include an area extending 1 to 2 cm. beyond the clinical margin of the growth. Element needles may be used in dosage of 100 to 130 mg.-hr. per cubic centimeter of tissue. The insertion of radium beyond the clinical margin of the growth has the purpose of "heading off" the peripheral infiltration. Deep external irradiation over the tumor and over the draining lymphatics to the extent of 1000 to 1200 mg.-hr. over each 2 sq. in. of skin surface, employing beta ray screen at 1 inch distance, should be employed, making use of all possible cross-fire. Intense irradiation with an applicator containing from 1 to 4 gm. at 6, 10 or 15 cm. distance, probably offers the best chance of success. Often, from 10 to 50 gm.-hr. may be given and repeated in six to eight weeks as indicated. The possibility of repeating applications is limited by fibrosis, decreased blood supply and atrophic skin conditions, factors which are apt to produce sloughing when the initial dose is reapplied.

Reaction. The general reaction is usually marked, especially if heavy dosage is given. This reaction begins at the time of application and lasts four to six weeks, depending upon the amount of destruction of malignant tissue. Malaise, anorexia, nausea, vomiting and headache are the common symptoms present. Free introduction of fluids to the extent of 40 to 50 ounces per day, free elimination, sufficient nourishment, and often blood transfusion, are valuable

measures employed in combating the general reaction. The local reaction is usually severe, being most marked when the interstitial method of application is used. The onset occurs within a few days, and is characterized by swelling, pain and redness, which reach their maximum during the third week. Shrinkage follows gradually, and continues, as a rule, until the sixth week. When deep external irradiation is used the onset is later, usually during the second week, with a gradual increase in the inflammatory reaction, often most marked during the fourth week. Then begins the decline and the decrease in size of the tumor. Recurrences may be evident as early as the sixth week. Complications are few, the most important being secondary pyogenic infection and thrombosis or embolism. Secondary growths may appear at any time after the second month. The favorable case terminates with a markedly reduced swelling which is but a fibrous remnant of the framework of the original tumor. No secondary growths are present and the mass remains quiescent.

Prognosis. The immediate prognosis is often good so far as one may judge by apparently complete local destruction of the mass. However, the growth usually recurs either *in situ*, in adjacent or in distant parts. Thorough roentgen-ray and clinical examination is indicated before treatment to rule out the presence of secondary growths. If they are found, there is no value to local treatment except as a mild palliative. In general, the prognosis in sarcoma is grave, almost hopeless.

Case History

Mr. K. Aged fifty-eight. Sarcoma of soft parts (small spindle-celled). Subcutaneous nodule removed one month previously. Prompt recurrence. Original site, border of right pectoralis major muscle. Two indurated masses in line of incision up to right axilla, measuring 3.0 by 2.5 by 1.0 cm., and 3.0 by 3.0 by 1.0 cm. Treated by 100 mg. radium, in form of 8 needles (13 per cent beta rays) homogeneously placed in masses for twenty-three hours. Total dose 2300 mg.-hr. Recurrence in four months. Same amount radium for eight hours (800 mg.-hr.). Also 100 mg. at 1 inch distance over two areas in axilla for fourteen hours, totaling 1400 mg.-hr. Total treatment, 6100 mg.-hr. Clinically well fourteen months.

References

Aikins, W. H. B. Sarcoma, following injury, successfully treated with radium. *Urol. & Cutan. Rev.*, 26: 33, 1922.

Aikins, W. H. B. Radium in sarcoma. *J. Radiol.*, 4: 44, 1923.

Andrews, C. F. Primary retroperitoneal sarcoma. Report of twenty-eight cases. *Surg., Gynec. & Obst.*, 36: 480, 1923.

Barbarin, P. The treatment of sarcoma. *Paris chir.*, 15: 421, 1923.

Keith, D. Y., and Keith, J. P. Three cases of sarcoma treated by radiation. *Am. J. Roentgenol.*, 9: 31, 1922.

Regaud, C., et al. Roentgenotherapy of sarcomas. *Paris méd.*, 51: 119, 1924.

Schreiner, B. F., and Herger, C. C. Radium and x-rays in the treatment of round-cell sarcoma. *Radiology*, 5: 399, 1925.

Vogt, M. E. Sarcoma of the uterus with a report of thirty cases. *Am. J. Obst. & Gynec.*, 5: 523, 1923.

Carcinoma of the Large Bowel and Sigmoid

Diagnosis is not discussed in this outline but should be established by roentgen-ray and clinical studies in every case and by biopsy when feasible. (See p. 13.)

Pathology. In the large bowel and sigmoid, columnar-celled carcinoma is the common form. It occurs most frequently at the flexures. Scirrhous types of slow growth are often seen, causing narrowing of the tract and stenosis. Linear and annular extensions are common. Bleeding, perforation and early metastases are not so common as in the fungating adenomatous lesions. In the latter the retroperitoneal lymph nodes and liver early become the sites of secondary growths.

Radium Indications. Frequently radium can be applied within the lumen of the bowel to these growths to advantage. The adjacent normal mucous membrane withstands irradiation well. Necrosis of the malignant cells can be secured with gamma rays. When laparotomy is done implants of radon may be inserted interstitially but the technic must be painstaking and very accurate.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The most common type of applicator is the long semi-rigid sound which may be introduced through a proctoscope, which has been passed into a colostomy opening or through the rectum. The application should carry

50 to 100 mg. or more of radium with a beta ray screen. The dosage tolerated lies between 1000 and 1500 mg.-hr. per 2 inch segment of lesion. The dosage should be modified according to the linear or annular character of the lesion, its thickness and the general condition of the patient. If a colostomy relieves the carcinoma-bearing loop of bowel from functioning, the dose may be higher than if fecal matter is continually passing over the ulcerated area during the period of the reaction. Accurate mensuration and sounding may give sufficient data for canalization in some cases when a colostomy has been done. In other instances the application had better be made under the fluoroscope with the aid of a barium mixture to identify the lesion. The location of the capsule must be checked by measurement or by the fluoroscope. The shaft of the applicator must be anchored by a lug or other suitable apparatus at the point of emergence to insure against any appreciable movement of the radiferous applicator away from the lesion. A large proctoscope with a mirror and an inflating bulb will enable one to pass a long-shafted applicator well up into the descending colon, make a visual application and be reasonably sure of its retention in place. A lug with thumb screw attachment can be firmly fastened snugly against the anus, and thus, by means of the semi-rigid shaft, the radium capsule can be retained against the lesion.

Such applications may well be supplemented by deep external irradiation over the abdominal wall through many portals of entry. One thousand milligram-hours at 1 inch distance over each 2 sq. in. of surface is a fair dose under ordinary conditions. Intensive irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance may be applied over the lesion, using many portals of entry. Such treatment probably offers the best prospect of success. When the radium therapy is done at the time of an abdominal section, implants of radon may be buried underneath the peritoneal coat, keeping in mind the danger of infection if the inserter is carried through the mucosa and again withdrawn, and remembering that it is better not to leave seeds within 0.5 cm. of the peritoneal surface. All in all, it seems best to employ the gamma rays delivered

from within the lumen of the bowel. Their action is slower and the necrosis comes about by autolysis, thus preserving the framework of the bowel. In the use of implants the destructive action is chiefly caustic in nature. Gold seeds carrying 1.0 to 2.0 mc. should be employed, depending upon the lesser or greater thickness of the induration. Subsequent applications can be made at intervals of six weeks if proctoscopic examination reveals incomplete destruction, extension, or at a later date if recurrences appear. The dosage may be repeated or adjusted according to the changed findings.

Reaction. The general reaction is usually not severe. Malaise with nausea and occasionally a degree or two of rise in temperature constitute the average reaction from a moderate dose of radiation administered within the large bowel. If a colostomy has been done, the reaction is mild. It often begins during the application and lasts intermittently for four weeks, being most intense in the third week if there is much tissue destruction and if no colostomy opening exists. Locally there is inflammatory swelling during the second and third weeks. Ulceration and slough rapidly follow and reach their maximum in the third week. With the fungating types of lesion, bleeding occurring during the few days following an application indicates trauma. Occasionally in the third week bleeding indicates erosion and at this time the complication of a perforation may have to be faced. Rarely perforation occurs from trauma at the time of application. By the fifth week repair is in progress, especially when a colostomy relieves the segment from the irritation of passing fecal matter. If a colostomy has not been made, repair is delayed, local reaction is prolonged, there is greater danger of slough and bleeding, and certainly the patient will experience pain, cramps, painful defecation and sometimes diarrhea when large doses are given.

Colostomy is indicated in all lesions when radium is to be depended upon for any real results in lower bowel carcinoma. Following resection, radium as a prophylactic agent may be passed into the involved area. Five hundred to 1000 mg.-hr. with beta ray screen and 1 cm. distance to each 2 inch segment of bowel will serve to inhibit recurrence. It

is best applied two to three weeks after resection or when the patient has fully recovered from the operation. Hemorrhage and perforation, which sometimes complicate the case during the third week, are much less likely to occur when a beta ray screen and much rubber for distance are used, even if the milligram-hour figures are high. If the dosage of radium therapy has been sufficient and successful, a pale, smooth, slightly scarred membrane with some telangiectasis replaces the normal rugated colonic mucous membrane. In successful cases this condition obtains by the eighth week. Cells lying deeper in the wall may be undestroyed and may be the cause of early recurrence or they may remain encapsulated in fibrous tissue for months before they ultimately regenerate. The function of the involved segment of the bowel may be impaired but seldom to such an extent as to cause serious symptoms. Constriction by scar tissue from annular lesions is to be feared.

Prognosis. The immediate results are often encouraging. Freedom from symptoms for many months and temporary arrest of the disease are often accomplished. Obstruction, bleeding, discharge or diarrhea are often relieved. Ultimately the growth recurs *in situ* or secondary growths become manifest in the retroperitoneal lymph nodes or in the liver, and the patient finally succumbs. In all but the most advanced cases, the palliative results are well worth the effort.

Case History

Mr. K. Aged seventy-three. Carcinoma of large bowel. Bleeding from rectum and symptoms of obstruction. Colostomy done three days before irradiation. Mass on posterior wall of sigmoid, ulcerated and adherent to sacrum. Treated with 100 mg. radium within involved segment for twenty-four hours with beta ray screen, totaling 2400 mg.-hr. Also 5280 mg.-hr. at 1 inch distance divided over four areas posteriorly opposite the lesion. Total dosage, 7680 mg.-hr. Marked symptomatic improvement. Reduction of mass beyond palpation. Well for three and one-half years.

References

Case, J. T. Suggestions regarding radium treatment of rectosigmoid carcinoma. *Am. J. Roentgenol.*, 14: 547, 1925.

Pinch, A. E. H. Carcinoma of the small intestine. A Report of the Work at the Radium Institute, London, Jan. 1, to December 31, 1922. *Radium*, N. S., 2: 58, 1923.

PINCH, A. E. H. Carcinoma of the large intestine. A Report of the Work at the Radium Institute, London, January 1, to December 31, 1922. *Radium*, N. S., 2: 58, 1923.

CARCINOMA OF THE STOMACH

Diagnosis is not discussed in this outline but should be established by roentgen-ray and clinical studies and by biopsy in every operative case. (See p. 13.)

PATHOLOGY. Adenocarcinoma of the pylorus or of either curvature is the most commonly encountered type of malignancy of the stomach. The medullary type early projects a fungating mass into the lumen. This type grows rapidly, metastasizes early to the neighboring lymph nodes and to the liver or extends to the head of the pancreas. Carcinoma simplex is of slower growth and extension. Scirrhous carcinoma infiltrates the stomach wall extensively, metastasizes late, and has the longest course, as a rule. Rarely an epitheliomatous type of growth develops about the cardia in prolongations of squamous-celled mucous membrane from the esophagus. Symptoms due to obstruction develop early in pyloric lesions. Bleeding is common from medullary types of growth while the scirrhous type may give little warning until extensive. Because of the concealed location and the obscure early symptoms, these all too common malignant lesions of the stomach are frequently not diagnosed until late in their course.

RADIUM INDICATIONS. Radium has not been used extensively in carcinoma of the stomach because of the mechanical difficulties of application. Operable cases are best treated surgically. Inoperable cases require repeated laparotomies if adequate radium applications are to be made under proper observation. To hope for permanent arrest of the disease, interstitial applications must be made to these lesions. Aside from burying radium within the tumor transperitoneally but two other methods are available. One, by placing of radium in the stomach through the mouth; and the other, by external irradiation through the abdominal wall. For successful radiation therapy the lesion must be accessible for application and fairly frequent observation. These conditions are difficult to obtain in carcinoma of the

stomach. Radium rays are capable of destroying or inhibiting malignant growth here as elsewhere. Cellular degeneration, necrosis, and healing can be made to occur. Fibrosis and endarteritis can be produced which will inhibit the course of the disease.

Complete regression is almost impossible because of the difficult mechanical and clinical problems.

The *contraindictions* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Gold radon implants of 1.0 to 2.0 mc. per seed may be buried deeply in the mass through an abdominal incision, using 1.0 to 2.0 mc. per cubic centimeter of malignant tissue. Element needles of various content can be inserted into the mass through the peritoneal coat, employing about 100 mg.-hr. per cubic centimeter of tumor tissue. Strong cords attached to the needles are allowed to protrude through an aperture in the abdominal wound, traction being made on these cords to remove the needles when the irradiation is completed. Implants, of course, are left in place and so the abdominal wound may be closed tight. At the end of six or eight weeks information regarding the situation obtained from fluoroscopic examination may be supplemented by exploratory laparotomy and reapplication of needles or implants may then be made if indicated. Powerful tubes may be passed into the interior of the stomach by means of semi-rigid applicators or tubes may be swallowed with strings attached. By means of manipulation of the semirigid applicator through the mouth or by traction on the attached string the tube may be brought into contact with the lesion under the guidance of the fluoroscope. Changes in position of patient or tube aid in irradiation of all parts of the lesion from within the stomach.

At best, the operator is working in the dark. A beta ray screen should be employed, and if possible, 200 to 300 mg. of radium must be available. It is better not to exceed a dose of 200 mg.-hr. per 2 sq. in. of surface, the total dose depending, of course, upon the size and extent of the lesion. A total of 1000 mg.-hr. within the stomach seems a safe dose. Such a method of application is of doubtful value. Cross-fire by

means of external irradiation over the lesion through the abdominal wall may be used to supplement the internal irradiation or it may be applied alone. With external irradiation alone, fair results might be obtained in susceptible tumors with from 1000 to 1200 mg.-hr. with beta ray screen at 1 inch distance over each 2 sq. in. of skin surface. This dose might be considered as a standard where only moderate amounts of radium are available. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance may be applied over the lesion, using many portals of entry. Such treatment probably offers the best prospect of success.

Reaction. When heavy interstitial irradiation is given the general reaction is marked. Malaise, nausea and vomiting in varying degrees may be present. When heavy external irradiation over the abdomen is given, the nausea and vomiting may be very severe. Anorexia and headache together with weakness may result in palpitation. Diarrhea is not uncommon and the picture of mucous colitis may last for several weeks. Blood has been seen in the stools when 30 or more gram-hours of radiation have been given, even in divided doses. Locally the extent of the reaction can only be conjectured, but it is probable that it consists of inflammatory reaction and destructive processes followed by repair and shrinkage. Evidences of the local reaction are seen in hematemesis and foul vomitus containing sloughing fragments of growth. Peritoneal irritation with pain follows irradiation close to the peritoneal coat. Fever as high as 101° to 102°F. is often present in severe radium reactions.

There should be manifest during the fifth and sixth weeks evidence of a lessening of the general reactions. When secondary anemia is present at the outset, it is apt to be aggravated by heavy irradiation, amounting to many gram-hours. Leucopenia may develop, and when the white blood count approaches as low a figure as 3500, all irradiation should be stopped and supportive measures emphasized. Blood transfusions are advisable preceding heavy radium treatments, especially when secondary anemia is already present; and they are indicated during the treatment if anemia threatens. Heavy fluid intake is of value, by hypoder-

moclysis if necessary, combined with stimulants, such as caffein, whiskey or general iron and bitter tonics. Sufficient caloric intake and rest in bed are imperative if the patient is to survive the reaction and keep up resistance against the vicious invader. In cachectic patients radium therapy is contraindicated in any but the mildest dosage, because the patient cannot endure the reaction; the absorption of toxic material has caused lowered resistance and has reduced ability to promote repair and to prevent recurrence. At the end of six or eight weeks careful clinical and roentgenologic examination may enable the radium therapist to determine upon further procedure. If the data are not sufficiently convincing, a laparotomy may be done, having the radium at hand to reapply if indicated. With carcinoma of the stomach, it is probable that radium is indicated only in inoperable cases; in such, the eventual outcome is evident and palliative effects are all that can be expected. When palliation only can be hoped for, the procedures already mentioned should be carefully considered and applications requiring such elaborate technic should be made only with the greatest hesitancy. The radiologist is working in the dark and the best clinical observation that can be made sheds only superficial light on the changes going on locally in the vital organs involved.

Prognosis. Permanent arrest of carcinoma of the stomach seems to be impossible with our present methods of radium application. Palliation brought about through relief of pain, healing of ulceration, prevention of hemorrhage, inhibition of growth, hindrance to the development of ascites, and general slowing of the course of the disease seem to be as much as can be accomplished under our present knowledge of radium technic. When combined with gastroenterostomy, the contribution of irradiation to the picture of improvement usually seen is difficult to estimate.

References

Levin, I. The intraperitoneal insertion of buried capillary glass tubes of radium emanation: results in two cases of tumor in the gastro-intestinal tract. *J. A. M. A.*, 79: 2074, 1922.

Menees, T. O. Intragastric radium treatment of carcinoma of stomach (radium applicator). *J. A. M. A.*, 86: 1904, 1926.

PARHAM, D. Colloid carcinoma. *Ann. Surg.*, 77: 90, 1923.
PINCH, A. E. H. Carcinoma of the stomach. A Report of Work at Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 56, 1923.
SOUTTAR, H. S. An address on radium and its surgical applications. *Brit. M. J.*, 1: 538, 1929.

CARCINOMA OF THE TONGUE

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. This lesion is characterized by a hypertrophic or excavating indurated ulceration, usually of the anterior portion, though the base is often the site of the lesion. The squamous-celled type is the most common. Leucoplakia often precedes the lesion. Metastases to the submaxillary and cervical glands occur rather early. The lesion is usually highly malignant.

RADIUM INDICATIONS. Radium is the therapeutic agent of choice. Complete necrosis of all malignant cells within the lesion is desired and apparently accomplished in successful cases. The ideal aimed at is complete destruction of the malignant tissue with a minimum of normal cell necrosis. Beta rays are most useful in accomplishing malignant cell destruction in these lesions. The immediate and end results from radium therapy excel those obtained by any other method. There is usually no disability, no immediate mortality, and no marked destruction of tissue; and the ready accessibility of the lesion renders the application of the radium and clinical observation relatively simple. In early cases the lesion responds to therapy by radium as well as by any other method and with a minimum of disfigurement. In advanced cases radium as a palliative agent has no peer.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. Interstitial application secures the best results, employing from 5 to 20 gold implants of 1.0 to 2.0 mc. per cubic centimeter of tissue. Second applications are only occasionally required. Element needles serve the same purpose in many cases, requiring around 100 mg.-hr. per cubic centimeter of malignant tissue. Platinum needles

allowing less than 5 per cent of beta rays to penetrate and containing but a few millicuries of radon, left in place many days, give great promise, thus prolonging the delivery of

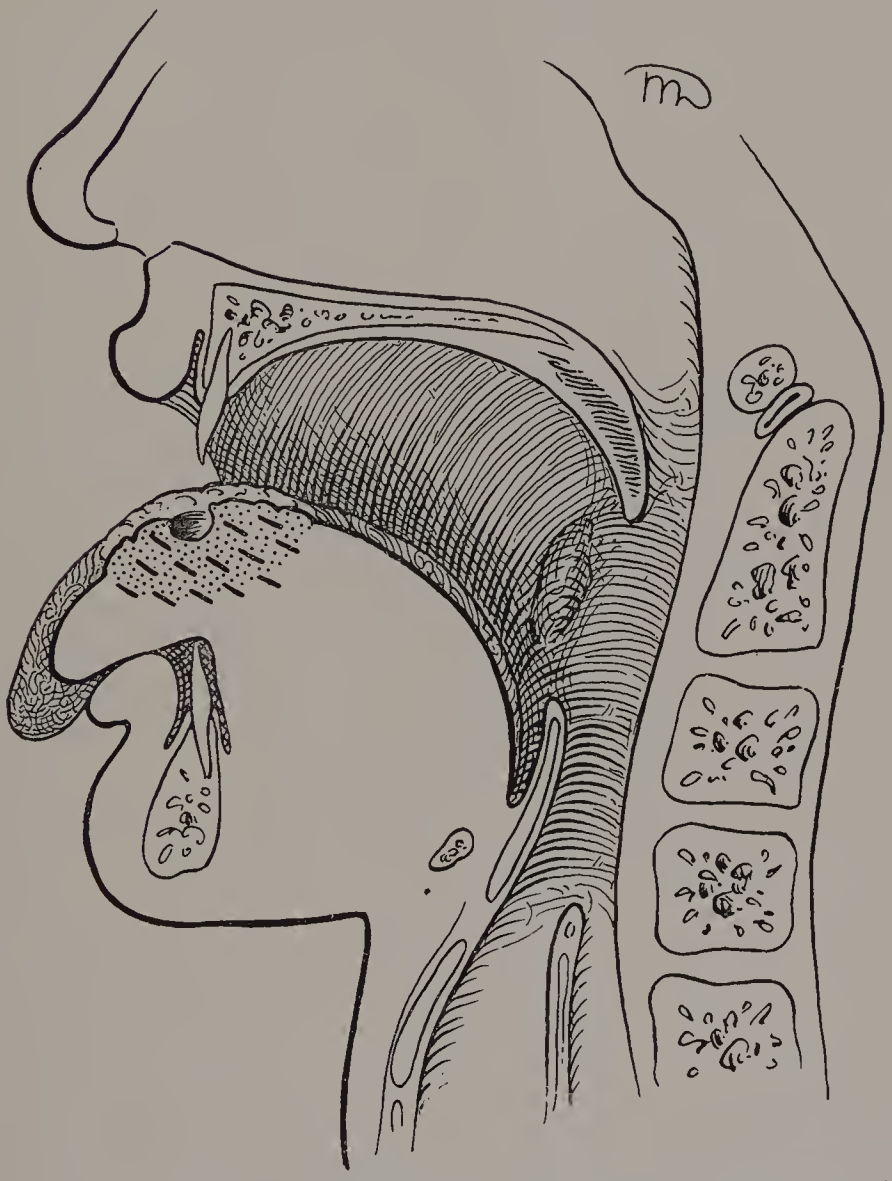


FIG. 27. Typical Radium Application in Carcinoma of Tongue. Lesion is studded with gold radon implants, 1 to 1.5 mc. each, placed 1 cm. apart and left permanently in tissues.

radium radiation to the lesion and tending to avoid a caustic action.

In European clinics platinum needles are inserted into carcinomata of the tongue and allowed to remain in place from four to seven days. The needles are inserted 1 cm. apart and in pairs with points together and eyelets opposed; the strings attached are tied together to hold the needles in place during the application. A string passed through a second eyelet is used to anchor the needle externally during the radiation and to withdraw the needle at the end of the treatment. From 140 to 160 mg.-hr. per cubic centimeter of malignant tissue are delivered during the radiation. Malignant glands in the neck and elsewhere are also treated by this method. These needles contain 1.33 mg. of radium per linear 15 mm. and are screened with 0.5 mm. of platinum.

Element needles containing 5, 10 and 12.5 mg., left in place for a few hours, are more commonly used in America. Formerly surface applications were employed, but destruction of malignant cells was not obtained to a sufficient depth, the surrounding normal mucous-membrane reaction was unnecessary and painful, and the duration of the reaction was increased.

The lymphatics draining the involved area should be irradiated in all cases, radically where palpable glands are present at the outset. This external irradiation should precede the interstitial application, since the sealing of the lymphatics may lessen the danger of embolic or traumatic dissemination by the implantation. One thousand milligram-hours per 2 sq. in. do very well. When metastatic gland involvement persists following irradiation, a second irradiation or surgical excision may be considered. When large amounts of radium are available, the dosage may be raised to 6 or even 10 or more gram-hours but this condition obtains only in the larger radium centers. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance over the lymphatics of the neck probably gives the best chance for favorable results. Radium is the only worth while agent where only palliation can be hoped for. External irradiations should not be given at shorter intervals than six weeks.

Reaction. When heavy gamma irradiation is given, there may be a marked general reaction, consisting of malaise, anorexia, occasional nausea and vomiting. Inter-

rupted irradiation, with an intermission of a few hours or days between applications, together with increased fluids, lessens the reaction. The general reaction lasts two to four or even six weeks. The primary reaction occurs while the radium is being applied and for two to three days thereafter. The secondary reaction is most marked during the third and fourth weeks, being much more marked when there is a considerable amount of tissue destruction and absorption. The local reaction consists of preliminary swelling and inflammatory reaction lasting from five to ten days followed by shrinkage. The onset occurs from two to five days after treatment. The shrinkage may be brought about by liquefaction and sloughing where ulceration is extensive, or by liquefaction and absorption where ulceration is slight compared to induration. Pain is present in varying degrees, and is often referred to the side of the face and up to the ear. It is more marked and prolonged when needles are used, and, as a rule, begins earlier. Gold implants are preferable. Pain interferes with eating and there is commonly noted a consequent loss of weight. About five weeks are required for the destruction, healing and replacement of the lesion by fibrous tissue when standard element needles or gold implants are used, but when glass radon implants are used, from eight to ten weeks are required, since these implants deliver caustic rays for thirty days after application. Extensive ulceration of normal mucous membrane takes place when surface applications are made to the tongue.

Prognosis. The prognosis is grave in any but the earliest cases. There is a fair chance of clinical cure in those lesions which measure less than 1 cm. in diameter or which have been present less than three months. In these groups metastases have not occurred and it is possible to eradicate the local lesion completely. In moderately advanced cases the local lesion may be destroyed but heroic measures must be instituted to overcome the glandular metastases. Heavy irradiation over malignant glands may cause them to shrink, but recurrence is likely. Surgical excision, preceded and followed by irradiation, is employed by some. Such patients may be made comfortable for one or two years. In advanced cases radium therapy offers the best chance for palliation,

reducing great sloughing ulcers, lessening foul discharge, prolonging the patient's ability to eat, and often allowing death to occur by gradual toxemia. Even in these cases pain is undoubtedly greatly lessened and true palliation accomplished. Advanced cases with metastases have been seen to recover clinically and live five years or more. Carcinoma of the tongue is rapidly coming to be considered as indicating the exclusive use of radium.

Case History

Mr. S. Aged fifty-five. Carcinoma of tongue. Indurated, ulcerated lesion, on dorsum of tongue. Biopsy. Leucoplakia for 3 to 4 cm. about the lesion. No enlarged glands. Treated by 62.5 mg. radium in needles (13 per cent beta rays) placed to produce homogeneous radiation about periphery of lesion for ten and one-half hours, totaling 630 mg.-hr. Reaction stormy. Patient alive and well two and one-half years later.

References

Boggs, R. H. Radium and deep therapy in the treatment of malignancy (carcinoma of tongue). *Radium*, 18: 49, 1922.

Fricke, R. E. A confusing inflammatory process due to implanting radium emanation tubes in the tongue. *Ther. Gaz.*, N. S., 39: 90, 1923.

Hanford, C. W. Cancer of the tongue under the influence of radium. *J. Radiol.*, 5: 55, 1924.

Janeway, H. H., Treatment of cancer, particularly of the tongue, tons and rectum by buried emanation. *Am. J. Roentgenol.*, 7: 92, 1920.

Judd, E. S. and New, G. B. Carcinoma of the tongue. *Surg., Gynec. & Obst.*, 36: 163, 1923.

Maunsell, R. C. B. Cancer of the tongue and floor of the mouth. *Med. Press & Circ.*, N. S., 99: 463, 1915.

Muir, J. Technic of use of removable radon seeds in carcinoma of tongue. *Ann. Surg.*, 83: 598, 1926.

Pinch, A. E. H. Carcinoma of the tongue. A Report of the Work at the Radium Institute, London, Jan. 1, to Dec. 31, 1922. *Radium*, N. S., 2: 50, 1923.

Quick, D. Treatment of carcinoma of the tongue. *Ann. Surg.*, 73: 716, 1921.

Quick, D. Radium treatment of carcinoma of tongue. *Brit. J. Radiol.*, 31: 81, 1926.

Regaud, C. On curietherapy of the epitheliomata of the tongue and of their subsequent adenopathy. *Brit. J. Radiol.*, 30: 361, 1925.

Schmidt, V. Sarcoma induced by roentgen-radium treatment of carcinoma of tongue. *Ugesk. f. Laeger.*, 88: 565, 1926.

Schreiner, B. F., and Brown, H. F. R. An investigation of the results obtained in cancer of the tongue treated by radium and roentgen rays. *Am. J. Roentgenol.*, 15: 207, 1926.

Simmons, C. C. Cancer of the tongue and mouth. *Am. J. Roentgenol.*, 13: 545, 1925.

Simpson, F. E. The treatment of cancer of the tongue by the implantation of bare glass tubes containing radium emanation. *J. Radiol.*, 6: 5–7, 1925.

Simpson, F. E. Radium emanation ampules in the treatment of cancer of the tongue. *Illinois M. J.*, 44: 139, 1923.

Simpson, F. E., and Flesher, R. E. Radium emanation in the treatment of cancer of the tongue and other parts of the oral cavity. *Am. J. Roentgenol.*, 15: 204, 1926.

Taussig, L. R. Carcinoma of the tongue and its treatment with radium. *Arch. Dermat. & Syph.*, 6: 424, 1922.

Tousey, S. Cancer of the tongue. *Am. J. Electrother. & Radiol.*, 41: 402, 1923.

Carcinoma of the Thyroid

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Adenocarcinoma of the thyroid gland is a rare but highly malignant form of growth. Early development is insidious. Extension by contiguity is rapid and distant metastases are common. Not infrequently distant secondary growths in the skeleton are the first clinical evidences of primary thyroid carcinoma. Infiltration is rapid; the capsule, the surrounding soft parts, the trachea and the esophagus are soon involved in one extensive mass of induration. Perforation or hemorrhage into these structures is not uncommon in late cases.

Radium Indications. Radium serves as the best palliative agent, for the diagnosis is seldom made while the growth is local and excisable. Radium therapy serves best whether one seeks local complete destruction or only temporary arrest. The lesion is accessible for external or interstitial application. Subsequent observations are easily made. Secondary growths so often complicate the picture that in advanced cases even the slightest attempt at palliation is of doubtful value. Irradiation is dangerous when there is narrowing of the esophagus or trachea, or when venous return is interfered with. The preliminary swelling accompanying the reaction may terminate the case suddenly.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. If the lesion is extensive, it is probably best to employ deep external irradiation only. The skin over the involved area may be divided into oblong areas

containing 2 sq. in. each. From 800 to 1200 mg.-hr. may be given over each area, at 1 inch distance, employing the beta ray screen. If more than three areas are irradiated on each side of the neck, the dosage to each area should approach the lower figure on account of the possible overlapping of irradiation by the more oblique rays. If the lesion is well localized, interstitial irradiation, employing radon or element needles, may be best. Gold implants containing from 1.0 to 2.0 mc. of radon, or element needles delivering from 100 to 130 mg.-hr. per cubic centimeter of malignant tissue will destroy the malignant cells within the area if the radiation is homogeneously distributed. Applications are best made through a surgical incision which exposes the lesion and insures accurate implantation. It is probable that surgical excision is attempted more often in early localized growths. In that event, radium applications in the form of gold implants of 1.0 to 2.0 mc. strength or element needles or gamma ray screened tubes should be made to the base of the wound to aid in the prevention of recurrence. Heavy dosage, however, may result in delayed healing or permanent sinus formation.

If distant secondary deposits are found, only the simplest of palliative treatments are advisable. Extensive clinical and roentgenologic examination should be made of all patients before any radical radium treatment is applied to carcinoma of the thyroid. Attempts at total eradication of local carcinoma of the thyroid gland are unjustifiable in the presence of distant secondary growths. Deep external irradiation may be repeated in five or six weeks. Bronzing of the skin is not uncommon. Successive doses should be reduced if the same portals of entry are employed. Interstitial treatments may be repeated in six or eight weeks, remembering the decrease in the formerly normal tissue tolerance and the apparent increase in tolerance to radiation on the part of the malignant cells.

Reaction. The general reaction in interstitial irradiation in carcinoma of the thyroid is usually mild. If 6 or more gram-hours of external irradiation are given, then there occurs an evident general reaction, characterized by malaise, nausea and occasional vomiting. This general reaction may

come on during the application and may last several weeks, depending upon the extent of destruction and subsequent absorption of malignant tissues.

The local reaction, which begins almost immediately in interstitial applications, is characterized by inflammatory swelling and local edema, followed by the disintegration of the more susceptible cells and their replacement by fibrous connective tissue. When element needles are used this process goes on during the first three weeks and is usually complete by the fourth or fifth week; it is slightly prolonged, though not so marked, when gold implants are employed. Dysphagia, dyspnea, or simply a feeling of fullness or a drawing sensation in the region of the thyroid gland are the common symptoms complained of by the patient. The severity of the symptoms referable to the local changes depends upon the degree of pressure present before the treatment and upon the degree of inflammatory swelling produced by the radium. Only in advanced cases with marked peritracheal involvement may tracheotomy be required. It is possible for a perforation into the trachea or esophagus to occur from placing interstitial applicators too near these structures. Subsequent contraction of fibrous tissue following extensive tumor destruction may distort the trachea or esophagus, thereby interfering more or less with their function, but ordinarily the sensation is only that of a drawing or constriction of the parts about the glands. Satisfactory end results would be indicated by a reduction of the mass to a fibrous remnant which remains quiescent for several months. Local recurrences may appear at any time or extensions to adjacent structures may be seen within a few weeks. Distant metastases are always a possibility in carcinoma of the thyroid.

Prognosis. Advanced cases with capsular and periglandular involvement are eventually hopeless. Worthwhile palliation, however, may be obtained by the careful use of extensive irradiation. Localized early carcinoma of the thyroid gland is rarely discovered except at the time of operation. If the malignancy is demonstrated at the time of operation, the burying of radium within the wound delays recurrences and inhibits growth. When distant metastases

are found threatening vital functions radium therapy may delay or inhibit these growths, thus prolonging life. Radium may be used to relieve pain only, thus affording temporary relief. The ultimate prognosis in carcinoma of the thyroid gland is grave in all instances.

Papilloma of the Bladder

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. These lesions are single or multiple, occurring at any age, and are prone to malignant degeneration. The growths are usually villous in type, but they may be pedunculated, sessile, or flat, and warty in character. The tumor consists of a fine or coarse bulky stroma covered usually with flat epithelial tissue resembling the bladder mucosa, though occasionally polygonal or cylindrical cells are found. Atypical epithelium with variegated forms suggests malignancy. Papillomata arise about the orifices of the bladder and around the edge of the trigone. The course of the disease lasts from a few weeks to many years. A quarter or more of these growths become malignant. Often the microscope is required to reveal their true nature. Bleeding, ulceration, infection and rarely extensions occur in papillomata of the bladder. These lesions may well be considered "precancerous." Susceptible bladder mucous membrane under the same etiologic environment predisposes to a multiplicity of the lesions and their recurrence after destruction.

Radium Indications. The frequency of malignant degeneration in papillomata of the bladder indicates the need of free use of radium rays to destroy the base of these growths to inhibit the regrowth of benign tumors, and to forestall the development of malignancy. Mechanical or physical measures are commonly employed to destroy these hypertrophic growths and they should be followed by irradiation to the base of the lesion. The susceptibility of papillomatous tissue and precancerous cells to radium rays has repeatedly been demonstrated. Therefore, treatment of papillomata of the bladder is incomplete without the inhibitory effect of radium rays accurately applied to the base of the lesion.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Either the surface or the interstitial method of application is available for use in papilloma of the bladder. If a cystotomy has been done, both methods may be employed. If the bladder is closed, the operative cystoscope in expert hands may be used to place the radium against the base of the lesion or it may be used for the insertion of element needles or radon implants. Surface treatment may be applied with lightly screened or unscreened radium, employing 15 or more per cent of the beta rays, giving 10 to 20 mg.-hr. per square centimeter of surface, or 50 to 75 mg.-hr. per square centimeter of surface when using only gamma rays. The insertion of element needles or gold implants to the extent of 1.0 to 2.0 mc. per square centimeter, or 20 to 50 mg.-hr. per square centimeter of surface, if the element needles are employed, may be considered as average dosage. Ordinarily such applications can be made easily in the open bladder without fear of distressing reaction. In the closed bladder the dosage should be reduced on account of the marked cystitis which follows the irradiation of large areas. It is perhaps best to give the radium treatments at a single seance, either in the open or closed bladder. Subsequent treatments may be given as indicated several weeks or months later.

Reaction. The general reaction is usually mild unless large areas are irradiated heavily. In that event malaise, anorexia, and nausea may be present. Locally the onset of the reaction is characterized by an inflammatory swelling, disintegration, liquefaction and slough of the base of the lesion, due to the caustic action of the beta and gamma rays. When the dosage has been accurately adjusted to the thickness of the bladder wall, the danger of perforation is slight. It is advisable to secure sloughing of the first 2.0 or 3.0 mm. of the lesion. At the end of three or four weeks the destructive process is complete and healing rapidly follows. In the open bladder, drainage is free and irrigation easy. In the closed bladder, the distress from cystitis is often severe, occasionally requiring sedatives. In many cases almost daily irrigation

is necessary. By the end of the fourth or fifth week, the reaction has subsided, and by the sixth week, as a rule, healing is almost complete. Recurrences are not uncommon, appearing from a few months to many years after the treatment. Complications in the nature of ascending infection may be troublesome. Favorable cases terminate with complete healing of the bladder mucosa and without recurrences at the site. Unfavorable cases develop multiple recurrences or degenerate into serious malignant growths.

Prognosis. When benign papillomata of the bladder are destroyed by physical or mechanical means, they frequently give no further trouble. The tendency of these lesions to become malignant indicates the use of some measure to prevent cancerous development. Radium furnishes the most suitable means of combating the malignant degeneration of papillomata of the bladder. Progress in the control of malignancy can well be accomplished by such agents as radium.

References

Souttar, H. S. An address on radium and its surgical applications. *Brit. M. J.*, 1: 538, 1929.

Heidler. Dissecting gangrenous cystitis due to radium. *Wien klin. Wchnschr.*, 40: 571, 1927.

Keyes, E. L. Treatment of bladder tumors with metal seeds containing radium emanation. *J. M. Soc. New Jersey*, 23: 485, 1926.

Morson, A. C. Radon therapy of vesical carcinoma. *Brit. J. Radiol.*, 32: 309, 1927.

Carcinoma of the Bladder and Prostate

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Malignant lesions in the urinary bladder are commonly of the squamous-celled variety. Papillomata are frequently the site of malignant degeneration. The bladder wall proper is often the site of carcinoma. The carcinomatous lesions commonly found are the flat infiltrating types which invade the bladder wall. Pain in the bladder, a feeling of fullness, and bleeding are frequent manifestations of malignant disease. Secondary growths are not common but they are occasionally found in the retroperitoneal lymph nodes. The bladder is not infrequently

the site of secondary growths from primary lesions in the prostate, rectum and uterus. In the prostate the adenocarcinoma arises within the gland, extending and enlarging to involve the capsule and later the bladder wall. The lesions bleed and by their enlargement obstruct the urinary flow. Greater hardness and a more rapid course are the common points of distinction between benign hypertrophy and carcinoma of the prostate gland. In early cases, while the malignant nature may be suspected, it is often only demonstrated upon section. Distant secondary growths are common and the skeleton is a frequent site.

Radium Indications. The use of radium has greatly improved the rather unsatisfactory treatment of bladder malignancies. It has proved most valuable as a means of palliation but when combined with surgical measures it has increased the percentage of cures. It has inhibited recurrences and accomplished palliation for many months longer than surgical measures alone. The application of radium and observation of the lesions are relatively simple. Cystoscopic technic has greatly widened the scope of radium service in the bladder.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Applications may be made through the rectum, the urethra, the perineum, operating cystoscopes, cystotomy incision, or externally over the suprapubic region or perineum. These methods of approach in various combinations offer cross-fire which greatly facilitates proper irradiation of lesions of the urinary bladder. External applications require large quantities of element or radon. Urethral and rectal applicators are usually in capsule form. Element or radon needles may be used through the perineum or by direct vision through the cystotomy incision. Large quantities of radon in small bulbs may be used through cystotomy incisions, rarely through the cystoscope; and implants may be inserted through the perineum, operating cystoscope or cystotomy incision. Complete necrosis by cautery action of bare radium or by autolysis from the use of screened radium is efficient in destroying or inhibiting the growth. The

method to be used depends upon the pathology and clinical aspects of the individual case.

The early applications of radium to bladder lesions were made by passing the capsule through the urethra on a sound, employing a beta ray screen. The capsule was placed more or less blindly in approximation to the lesion. Three hundred to 600 or 800 mg.-hr. were thus given. Such applications in late neglected cases will stop the bleeding and delay the growth, especially if combined with gamma ray rectal or vaginal applications amounting to 600 to 1200 mg.-hr. and external irradiation over the suprapubic area.

In bladder malignancies it is advisable to make all applications if possible by direct vision through a suprapubic cystotomy incision. Then the applications can be accurately made, packing the capsule or capsules firmly against the lesion. Flat infiltrating lesions are perhaps best treated by surface irradiation, employing gamma rays only, or in some cases 10 per cent of the beta rays also. Homogeneous irradiation over the surface of the induration and for a distance of 1 cm. beyond, in dosage of 200 to 400 mg.-hr. per square inch, constitutes a fair application. Element needles or radon implants may be used in thickened or raised lesions. One to 2 mc. gold seeds per cubic centimeter, kept more than 0.5 cm. from the external bladder wall, serve to destroy malignancy, chiefly by necrosis. Element needles of various sizes may be used homogeneously 1 cm. apart and 0.5 cm. from the external bladder wall. One hundred milligram-hours per cubic centimeter of tissue is an average dose. Fulguration of suspicious papillomatous lesions is strongly advocated, followed by surface irradiation of the base to the extent of 300 to 400 mg.-hr. per square inch, using beta ray screen. Implants may be placed in intravesical tumors through the operating cystoscope with an implanting puncture needle designed for the purpose. The dosage should be less than when a cystotomy has been done on account of the reduced freedom of drainage and impeded passage of sloughing material. Irradiation cystitis in the closed bladder may be a distressing experience for the patient. Fulguration, to be followed by surface irradiation with large amounts of radon in a bulb, may be done

through the operating cystoscope but the surgeon must have experience and dexterity of high degree. Irradiation is best done after the slough has completely separated.

In carcinoma of the prostate, intraglandular lesions are commonly removed surgically. Subsequently the cavity should be irradiated with gamma ray applicators to the extent of 600 to 1200 mg.-hr., depending upon the size of the cavity. This irradiation is best given through the cystotomy incision by direct vision and with the capsule or capsules packed firmly in place.

Carcinoma of the prostate which has extended to the extraglandular tissue is best treated by interstitial radium application. The method of choice is implantation through a cystotomy incision. Element needles or gold implants serve the purpose, with a recommended dosage from 90 to 130 mg.-hr. or mc.-hr. per cubic centimeter of malignant tissue. Rarely implantation of the seeds may be accomplished homogeneously through the operating cystoscope. Perineal approach can well be employed when the diagnosis is assured and cystotomy is contraindicated or refused. Through perineal incisions, with the examining finger in the rectum serving as a guide, long element needles may be inserted into the prostatic mass or gold implants may rarely be homogeneously lodged in the malignant growth. In any event interstitial application is best supplemented by rectal or vaginal application and deep external irradiation from the suprapubic area. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance through several portals of entry probably gives the best promise of success. Due allowance must be made for the interstitial and local irradiation.

In all prostatic malignancies the presence of secondary growths and especially those in the skeleton must be ruled out before radical therapy is instituted. If distant secondary lesions are found, the local treatment should be palliative only. The method of application selected should be the one least disturbing to the patient and the one best suited to the individual patients, all things being considered. Applications can be repeated or supplemental treatments given six to eight weeks later, due regard being given to fibrosis,

impaired local circulation and, of course, the general condition of the patient. All sloughing and inflammatory reaction should have subsided before reapplication. The open bladder with free drainage permits earlier repetition of radium therapy. As a rule, when the bladder is secondarily involved from cancer of other organs, palliation is all that can be hoped for and the radium therapy is devised with that object in view.

Reaction. In general the reaction from radium treatment in the open bladder is not severe. Free drainage greatly reduces absorption. If heavy external, rectal or vaginal irradiation is given, the general reaction increases accordingly. General malaise and depression constitute the ordinary reaction. If the irradiation has been applied to the unopened bladder, the reaction is usually more severe, although probably secondary to genitourinary tract disturbances. Toxic absorption is increased; free drainage is not obtained if urination is painful because the patient hesitates to take the copious amounts of fluid needed. Frequent, painful urination greatly disturbs the patient, thus increasing the reaction. If obstruction develops, catheterization, or even a cystotomy, may have to be resorted to eventually. Locally the reaction begins from five to fifteen days after treatment, earlier in the interstitial applications, and later when the gamma ray surface applications have been made. Swelling plays a large part in causing an unpleasant reaction, and especially in prostatic lesions; partial or complete obstruction may follow the radium treatment. Disintegration and sloughing, which comes chiefly in the third week, tax the closed bladder heavily. Catheterization and frequent irrigation may be employed for relief during the height of the reaction. Regression begins by the fourth week, and may require three or four weeks for completion. Healing may occasionally be delayed to the twelfth week or even longer.

With the open bladder, irrigation and increased fluid intake greatly reduce the systemic reaction. Hemorrhage from trauma may immediately follow treatment. It is seldom severe or fatal. Late secondary hemorrhage from erosion by the radium rarely occurs. Perforation of the organ is uncommon; when it occurs, it is the result of rapid gamma

ray destruction of the completely involved bladder wall, or from excessive action of interstitial application which may have been too severe or too close to the external bladder wall. Kidney or ureteral lesions may occasionally develop in closed bladders, caused by obstruction. Satisfactory results in the end present a smooth, slightly scarred wall, non-ulcerated, slightly injected, and perhaps distorted, but not seriously interfering with function. In prostatic lesions the contraction and fibrosis may increase the obstruction, especially if the middle lobe is involved. Catheter life may be the result or a permanent cystotomy may be necessary, if obstruction is complete and persistent.

Prognosis. In almost all types of carcinoma of the bladder and prostate the immediate results are encouraging. Partial or apparently complete regression is often obtained in the moderately advanced and early cases. Each lesion must be treated on its own indications, and reacts in its own manner. Results are thus varied. The various methods of access and dosage must be adapted to the individual case in hand. Many local and general factors enter into the selection of the best method of attack. Complete regression or fibrotic encapsulation with relative comfort and clinical freedom from the disease for months or even years is occasionally accomplished. If the patient is kept under close observation and if frequent cystoscopy is done, recurrences are discovered early and re-treatment is promptly given. The majority of the cases, however encouraging they may be at the beginning, eventually die of the disease, the bladder wall cases from local recurrence and extension, and the prostatic cases often from distant secondary growths. Radium seems not to have greatly improved the remote results, but it has undoubtedly improved the immediate and palliative treatment of carcinoma of the bladder and prostate.

Case History

Mr. P. Aged fifty-seven. Carcinoma of prostate. Mass, size of grapefruit, enucleated from site of prostate. Biopsy. Treated with 100 mg. radium, packed for twenty-four hours into depression left after removal of mass. Beta ray screen. Clinical recovery in four months. Gained 35 pounds. Well one and one-half years.

References

Alamartine and Charleux. Treatment of a degenerated papilloma of the bladder by radium. *J. d'urol. méd. et chir.*, 16: 291, 1923.

Ayres, W. Radium in cancer of the bladder. *N. York M. J.*, 101: 345, 1915.

Barringer, B. S. Radium treatment of carcinoma of the bladder. *Ann. Surg.*, 74: 751, 1921.

Barringer, B. S. Carcinoma of prostate. *Surg., Gynec. & Obst.*, 34: 168, 1922.

Barringer, B. S. Radium versus surgical removal of carcinoma of the bladder. *J. A. M. A.*, 79: 1504, 1922.

Barringer, B. S. Technic and statistics in the treatment of carcinoma of the bladder by radium. *Am. J. Roentgenol.*, 9: 757, 1922.

Barringer, B. S. Radium in the treatment of prostatic carcinoma. *Ann. Surg.*, 80: 881, 1924.

Barringer, B. S. Radium removal of carcinoma of the bladder. *J. Urol.*, 13: 131, 1925.

Barringer, B. S. End-results of radium removal of carcinoma of the bladder. *J. A. M. A.*, 90: 352, 1928.

Braasch, W. F. Tumors of the bladder and their non-operative treatment. *Minnesota Med.*, 1: 168, 1918.

Buerger, L. The cystoscopic application of radium. *Radium*, N. S., 1: 99, 1922.

Buerger, L. New method of application of radium by means of a cystoscope. *J. d'urol. med. et chir.*, 14: 409, 1922.

Buerger, L. A new method of applying radium through the cystoscope. *J. Urol.*, 9: 227, 1923.

Buerger, L. Radium in carcinoma of the bladder. *Urol. & Cutan. Rev.*, 27: 213, 1923.

Bugbee, H. G. Experience with radium in cancer of the prostate. *J. Urol.*, 6: 459, 1921.

Bugbee, H. G. Report of cases of malignant growths of the bladder treated by resection and radium. *J. Urol.*, 10: 159, 1923.

Bumpus, H. C., Jr. Radium in cancer of the prostate. *J. A. M. A.*, 78: 1374, 1922.

Burnam, C., and Walker, G. Cancer of the urinary bladder cured by radium. *J. A. M. A.*, 80: 1669, 1923.

Burnam, C. F., and Neill, W., Jr. The treatment of epithelial tumors of the bladder. *Am. J. Roentgenol.*, 16: 219, 1926.

Clark, J. G., and Keene, F. E. Radiation in inoperable cases of carcinoma in the female genito-urinary organs. *Am. J. Roentgenol.*, 7: 36, 1920.

Clark, J. G., and Keene, F. E. Irradiation in cancer of the female genito-urinary organs. (Results in three hundred and thirteen cases.) *J. A. M. A.*, 77: 613, 1921.

Cunningham, J. H. The treatment of carcinoma of the prostate. *Boston M. & S. J.*, 186: 99, 1922.

Deming, C. L. Results in one hundred cases of cancer of prostate and seminal vesicles treated with radium. *Surg., Gynec. & Obst.*, 34: 99, 1922.

Frank, W. Cancer of the prostate gland treated by radium. *Kentucky M. J.*, 20: 603, 1922.

GERAGHTY, J. T. The results of treatment of bladder tumors. *J. A. M. A.*, 69: 1336, 1917.

GERAGHTY, J. T. Value of radium in the treatment of bladder tumors. *South. M. J.*, 13: 511, 1920.

GERAGHTY, J. T. Treatment of malignant disease of the prostate and bladder. *J. Urology*, 7: 33, 1922.

GOIN, L. S. Radiation therapy of malignant bladder tumors. *Urol. & Cutan. Rev.*, 28: 269, 1924.

GOUVERNEUR, R., and FABRE, S. Lesions of the bladder in carcinoma of the uterus before and after radium therapy. *Bull. Soc. d'obst. et de gynec. de Paris*, 13: 782, 1924.

HERBST, R. H.Blocking lymphatics in the control of carcinoma of the prostate gland. *J. A. M. A.*, 82: 1590, 1924.

HYMAN, A. The intravesical treatment of carcinoma of the bladder by implantation of radium emanation tubes. *Surg., Gynec. & Obst.*, 39: 827, 1924.

IBANEZ. High frequcncy treatment and deep roentgenotherapy in malignant tumors of the bladder. *Rev. méd. cubana*, 35: 263, 1924.

JECK, H. S. Apparent cure of carcinoma of the bladder. *Internat. J. Surg.*, 32: 240, 1919.

KOLISCHER, G., and KATZ, H. Radium in malignant tumors of the bladder and prostate. *Urol. & Cutan. Rev.*, 27: 218, 1923.

KEYES, E. L. Malignant tumors of the testicle. *Am. J. Roentgenol.*, 15: 44, 1926.

KEYES, E. L. Principles governing the local treatment of carcinoma of the bladder. *J. A. M. A.*, 90: 350, 1928.

LEVIN, I. The relative position of surgery, radium, and x-ray therapy in carcinoma of the prostate and bladder. *Urol. & Cutan. Rev.*, 28: 392, 1924.

MARION, G. The hemostatic action of radium in tumors of the bladder and urethra. *J. d'urol. méd. et chir.*, 13: 161, 1922.

NEILL, W., JR. Radium in the treatment of new growths of the male bladder. *J. A. M. A.*, 79: 2061, 1922.

ORAISON, J. Cancer of the prostate and radium. *Bull. Soc. franc. d'urol.* 1: 209, 1922.

ORAISON, J. Tumors of the bladder and radium therapy. *Bull. Soc. franc. d'urol.*, 2: 161, 1923.

OSGOOD, A. T., and CAMPBELL, M. F. Some of the clinical aspects of cancer of the prostate and bladder. *Arch. Clin. Cancer Research*, 1: 59, 1925.

PASTEAU, O., and DEGRAIS. The employment of radium in the treatment of cancer of the prostate. *J. d'urol., med et chir.*, 4: 341, 1913. Eng. Transl., *Canad. Pract. & Rev.*, 38: 703, 1913.

PERRIER, C., and ANDREAE. The treatment of prostatic carcinoma by radium. *J. d'urol. med. et chir.*, 13: 15, 1922.

SCHNOEBELEN, P. C. Management and results of deep therapy in tumors of the bladder and prostate. *J. Missouri State M. Ass.*, 22: 57, 1925.

SCHOENENBERGER, F. J., and SCHAPIRA, S. W. Application of radium in the bladder for carcinoma with report of two cases. *J. A. M. A.*, 63: 1852–1914.

SCHOLL, A. J., JR., and BRAASCH, W. F. Pre-operative treatment of malignant tumors of the bladder by radium. *Arch. Surg.*, 5: 334, 1922.

Smith, G. G. Radium in cancer of the bladder. *Surg., Gynec. & Obst.*, 33: 570, 1921.

Smith, G. G. The management of cancer of the bladder. *Boston M. & S. J.*, 187: 97, 1922.

Smith, G. G. The treatment of cancer of the bladder by radium implantation. *J. Urol.*, 9: 217, 1923.

Smith, G. G. X-ray and radium therapy in urology. *Boston M. & S. J.*, 192: 335, 1925.

Squier, J. B. Radium versus surgery in the treatment of vesical neoplasms. *Surg., Gynec. & Obst.*, 21: 176, 1915.

Thomas, B. A., and Pfahler, G. E. Technic of the treatment of carcinoma of the bladder and prostate by a combination of surgery, electrocoagulation, radium implantation and roentgen ray. *Arch. Surg.*, 4: 451, 1922.

Waters, C. A. The new type of high voltage roentgen therapy in the treatment of carcinoma of the bladder. *Am. J. Roentgenol.*, 11: 19, 1924.

Watson, E. M. A technique for the application of radium emanation in carcinoma of the prostate. *Bull. Buffalo Gen. Hosp.*, 2: 19, 1924.

Watson, E. M., and Herger, C. C. A technique for handling prostatic carcinoma. *J. Urol.*, 13: 343, 1925.

Young, H. H. The use of radium in cancer of the prostate and bladder. *J. A. M. A.*, 68: 1174, 1917.

Young, H. H., and Frontz, W. A. Carcinoma of the genito-urinary tract. *J. Urol.*, 1: 505, 1917.

Young, H. H. Technic of radium treatment of cancer of the prostate and seminal vesicles. *Surg., Gynec. & Obst.*, 34: 93, 1922.

Prostate Gland (hypertrophy)

Diagnosis is not discussed in this outline, but should be established by every possible means. (See p. 13.)

Pathology. Chronic enlargement of the prostate gland is common in men past sixty years of age. Grossly, the structure of the enlarged prostate gland may be smooth or irregular, homogeneous or unevenly nodular; most commonly the so-called middle lobe is involved. Obstruction to the free passage of urine from the bladder usually results from prostatic hypertrophy. The middle lobe may act as a valve, causing urinary stasis, secondary infection, ascending in type, and resulting in serious upper genitourinary tract pathology. Histologically there is fibrous connective tissue thickening and hypertrophy with or without increase of muscle fiber. Tumors composed of pure muscle fiber are rare. Glandular structures may be hypertrophied, with multiple cyst formation, sacculations, and involvement of irregular isolated areas.

The vicinity of the prostatic ducts is the most frequent site of the fibrous hypertrophy. The lesion may include fibrous, muscular, and glandular elements in varying proportions. Retention cysts, with concretions, dense fibrosis, and sclerosis, are common in chronic lesions. Malignant degeneration is a not uncommon microscopic finding in clinically benign growths. A common finding is simple adenoma in which the glandular hypertrophy predominates. That hypertrophy of the prostate is due to chronic inflammatory changes, the result of a reaction against long-continued irritation, sums up the general view.

Radium Indications. In an increasing number of instances radium radiation produces atrophy and decrease in the size of the hypertrophied prostate gland. Several biological effects of radium may be active in these results. The obliterative endarteritis may decrease the blood supply, thus starving the adenomatous overgrowth. Dense fibrous overgrowth may be replaced by fine connective tissues under the influence of the rays. Muscular, as well as fibrous and glandular, hypertrophy may be reduced by the action of the rays which destroy or inhibit the growth of proliferating cellular structures here as elsewhere in the body. Dense fibrous enlargements with sclerotic changes are but little affected by radium rays. Cystic processes are only slightly influenced, and old calcified areas are unaffected by the radium. When the cellular nature of the prostatic enlargement is not known, the use of radium may be attended with discouraging results. If the lesion is a simple adenoma or a relatively early fibrous or muscular hypertrophy, the use of radium may be attended with surprising degrees of success. Heavy irradiation of the prostate in a bladder markedly inflamed is apt to be followed by a reaction which may be severe, requiring frequent irrigation, sedatives, and permanent catheterization, but rarely necessitating cystotomy. The significance of radiation cystitis as a complication must be kept in mind when considering the radium treatment of hypertrophy of the prostate.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Surface, cavity, interstitial and deep external methods of application are all useful for the treatment of hypertrophy of the prostate. The interstitial application of element or radon needles or implants yields the best results, but requires more complicated technic. Access may be gained through the perineum, through the urethra by means of an operating cystoscope, or through the rectal mucosa, the latter avenue of approach being but little employed. Long shanked needles inserted through the perineum, under a local anesthetic, are perhaps most commonly employed for interstitial insertion. Intraurethral implantation is to be avoided except when gold implants are available. There is an uncertainty when working blindly and this must be taken into account when one decides to employ this method of application. Entrance through the urethra by means of an operating cystoscope is used by experts in cystoscopy. The dosage should be 0.5 mc. per cubic centimeter if glass implants are used, or 1.0 to 2.0 mc. if gold implants are used, or from 50 to 100 mg.-hr. per cubic centimeter if needles are used, permitting the passage of 10 to 15 per cent of the beta rays. Intraurethral applications may be made by passing a radium capsule attached to a sound into the prostatic urethra and employing gamma rays in the amount of 200 to 400 mg.-hr. per linear inch. Rectal applications, heavily screened, may be placed against the palpable prostate at 1.0 cm. distance, delivering 800 to 1200 mg.-hr., without serious damage to the rectal mucosa. Deep external irradiation over the perineum or suprapubic region, employing gamma rays, may also be used. The latter method requires larger amounts of radium to deliver therapeutic doses of gamma rays to the lesion. A combination of interstitial, urethral, and rectal methods of treatment may be advisable, employing smaller dosage at each site. The effect will perhaps be greater on account of the effect of cross-fire. Applications may be repeated in from eight to ten weeks, except in the interstitial method where an attempt should be made to adjust the initial insertion to the desired therapeutic dose. Relief of symptoms as the result of the initial treatment may encourage the radiologist to further effort. No improvement

after eight to ten weeks in spite of adequate initial dosage discourages further radium treatment. In general, it may be stated that the initial treatment should be designed to deliver the full therapeutic dosage desired.

Reaction. Except in heavy interstitial applications in large prostates or in the case of multiple cross-fire applications amounting to several gram-hours, the general reaction is not severe. Malaise, nausea, and anorexia are not uncommon in 3 to 4 gm.-hr. treatments. Locally the reaction may be marked. Inflammatory swelling begins within a few days in the interstitial applications and within ten days where gamma rays only are used. Cellular and general glandular swelling may last for seven to ten days, followed by shrinkage and atrophy. There is necrosis about the needles or implants when they are inserted into the gland. Absorption and fibrous shrinkage follow. Atrophy of glandular, fibrous, and muscular tissues follows the treatment after six, eight, or ten weeks, and may continue for as long as six months. The bladder, in a case of an enlarged prostate requiring treatment, is frequently the site of chronic inflammation. This inflammation may be lighted up, causing a stormy reaction. Subsequent shrinkage of the gland may constrict the urethra, resulting in further obstruction, or at least interfering with relief from the obstructive symptoms. Increase in the obstruction not infrequently follows radium treatment, and it must be considered as a possibility.

Prognosis. A case of hypertrophied prostate gland, not suitable for surgical treatment, may be benefited by radium treatment. Radium is an agent capable of reducing the size and inhibiting the growth of enlarged prostates and its use should be kept in mind when other measures cannot be employed. By careful clinical study one should make careful selection of those cases which are structurally amenable to radium treatment. Old, fibrous, sclerotic, calcified or cystic lesions are very resistant to radium treatment.

Case History

Mr. T. Aged fifty-six. Hypertrophied prostate. Painful urination for one year. Pain on sitting and driving car. Enlarged prostate. Refused surgery. Treated by 600 mg.-hr. per rectum, with beta ray screen, at 3.0 mm. distance.

Marked flare-up of old cystitis. Reaction so severe that cystotomy was required. Removal of a small fibrosed shrunken prostate eight weeks after radium.

References

Bumpus, H. C. Radium in the treatment of benign hypertrophy of the prostate. *J. Urol.*, 12: 63, 1924.

Burnam, C. F. and Neill, W., Jr. The treatment of benign hypertrophy of the prostate with radium. *Urol. & Cutan. Rev.*, 28: 261, 1924.

Dennis, W. A. The use of radium in the treatment of benign hypertrophy of the prostate. *Minnesota Med.*, 6: 9, 1923.

Kogan. Hypertrophy of the prostate and radium. *J. d'urol. méd. et chir.*, 19: 23, 1925.

Varo Sweringen, B. and Cameron, D. F. Radium in simple hypertrophy of the prostate. *Internat. J. Med. & Surg.*, 36: 467, 1923.

Young, H. H. The use of radium and the punch operation in desperate cases of enlarged prostate. *Ann. Surg.*, 65: 633, 1917.

Carcinoma of the Maxillary Antrum

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The squamous-celled type of carcinoma is ordinarily present in the antrum, often associated with inflammation originating in a canine tooth, and occurring either preceding or following extraction. The cavity of the sinus fills with a soft vascular mass and gives symptoms from pressure and distortion of adjacent parts (palate, cheek, orbit or teeth). Metastases are not common but direct extension follows neglected cases.

Radium Indications. Radium in conjunction with mechanical measures is indicated. Entrance to the antrum must be obtained by cautery or extensive puncture, and the radium tubes inserted within the cavity if one hopes to obtain the best results. Radical surgical excision is mutilating, while radium may accomplish its purpose without visible disfigurement. Necrosis of all malignant tissue is sought, employing gamma and beta rays.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Radium tubes are commonly inserted through an opening in the canine fossa. Entrance may be obtained through the nose. A soft, bleeding mass usually

presents which may be cauterized and the radium application made a few days later when the slough has separated, or the radium tubes may be forced through the soft mass at the outset. Cauterization with subsequent radium insertion has frequently been employed. Packing is inserted with the tubes to maintain them in position. Careful aseptic technic is desirable in this as well as all forms of cavity application. Deep external irradiation over the cheek and the adjacent involved structures supplements by cross-fire the cavity treatments. One thousand milligram-hours over each 2 sq. in. of skin surface is a fair standard of dosage for ordinary conditions. Beta ray screen, at 1 inch distance, completes the technic of external irradiation. Element or radon inserted into the cavity, either in its approximate center in one tube or in several evenly distributed tubes, may be used. Light screening, permitting the passage of 10 per cent of the beta rays is advisable, for the numerous beta rays will cause complete necrosis within the cavity. This is the goal sought. Beta rays should always be employed when the radium is completely surrounded by malignant tissue. From 600 to 1800 mg.-hr. may be used in the antrum. If recurrence or incomplete destruction results, the dose may be repeated. However, a dosage above 2000 mg.-hr. within six weeks should be given advisedly. Subsequent applications may be given externally and internally if it is evident that the lesion is out of control. Extensive sloughs and severe reactions with possible permanent damage to normal structures, such as the eye, palate, and cheek, can occur and must be kept in mind.

Reaction. The reaction from adequate dosage in this location is usually severe. Cavity applications about the face, when malignant cell destruction and absorption are marked, result in malaise, nausea, vomiting, often an almost complete loss of appetite. Headache is added to the other symptoms. The reaction begins within a few hours after application and lasts intermittently three to four weeks. Infection may play a large part in reactions here. Free, open drainage lessens the reaction.

Locally, the reaction is marked by swelling and pain. The cheek, the eyelid, the palate and the maxilla are all affected.

These symptoms appear within the first few days and often last until the end of the third week. Discharge is profuse and increasing up to the third week, from which time it becomes thinner, less odorous, and less profuse. Should drainage not be free, local reaction is much increased. Complete necrosis and sloughing are usually accomplished by the end of the fourth week. Healing follows rapidly. A smooth, pale membrane indicates local destruction. Swelling of all adjacent parts subsides with the healing or before it. If no malignant tissue remains, fibrosis and shrinkage reduce the size of the cavity and the opening into it. Thus some approach to normal is brought about.

Prognosis. The prognosis is grave in any but the earliest cases, and early diagnosis is rare. Symptoms arousing suspicion arise from pressure; consequently the growth is already extensive when the diagnosis is made. Even in advanced cases, clinical cures lasting for many months or even years are not uncommon. Extensive sloughing of normal adjacent parts has been followed by recovery. The absence of early metastases very often reduces the task to one of local destruction only.

Case History

Mr. C. Aged sixty. Carcinoma of maxillary antrum. Curettement and removal of all diseased tissue possible. Postoperative irradiation consisting of 2400 mg.-hr. over site of lesion externally, using two areas at 1 inch distance, with a beta ray screen; also 50 mg. with beta ray screen packed in antrum for twenty-four hours, totalling 1200 mg.-hr. Total 3600 mg.-hr. Mild reaction without pain. Improvement locally and generally. Recurrence in six months. Died of the disease.

References

Blaisdell, J. H. Squamous cell carcinoma of the antrum. (Report of a case treated with radium alone, that is free from recurrence twenty-two months after the last application.) *Boston M. & S. J.*, 185: 570, 1921.

Greene, D. C. Carcinoma of the antrum. *Am. J. Roentgenol.*, 9: 591, 1922.

Janeway, H. H. The treatment of tumors of the superior maxilla. *Ann. Surg.*, 68: 353, 1918.

Johnson, F. M. Radium treatment of carcinoma of the antrum. *Surg., Gynec. & Obst.*, 38: 819, 1924.

New, G. B. Treatment of malignant tumors of the antrum. *J. A. M. A.*, 74: 1296, 1920.

Carcinoma of the Larynx

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The lesion is squamous-celled in type, more often intrinsic than extrinsic. It frequently has its origin on the cord or epiglottic folds and spreads over the interior of the larynx by thickening and fungating. Later, if left alone, it extends or metastasizes to the extralaryngeal tissues, producing an indurated mass in the neck with the larynx in the center. The latter picture is most common when the growth is extrinsic. Such masses combined with glandular metastases in the deep cervical lymphatics may be found in extrinsic carcinoma of the larynx even in cases where the interior of the larynx presents no induration, ulceration or other evidence of malignancy.

Radium Indications. Radium is the agent of choice for the treatment of carcinoma of the larynx because it can be accurately applied directly against or into the growth. When screening and dosage can be properly adjusted to the lesion, local eradication can be accomplished. Tubes of small size, containing radon or element, can be inserted into the larynx and laid against the lesion, employing a beta ray screen. Implantation of radon within the mass can be accomplished if the lesion is more extensive. By these means and by external irradiation from the sides of the neck, complete destruction of the lesion can be brought about. Laryngectomy is mutilating. However, with excellent surgical technic the curative results are superior to those with radiation. Surgery should be supplemented by ray therapy. The same result can be accomplished with radium alone without mutilating operations, and with a minimum of danger to the patient.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. A preliminary tracheotomy is justifiable in all radium treatments of carcinoma of the larynx; indeed, it may often be imperative during the period of reaction. For intrinsic growths, small, flat tubes serve best. They can be inserted into the larynx by the indirect method and

manually retained in place against the lesion. If small amounts only are available, the treatment may be given in series. Where large amounts of radon are at hand, the dose may be delivered at one sitting. Cocaine locally and morphine hypodermatically are valuable aids in promoting the comfort of the patient and the accuracy of application and retention of the tubes in place. The dosage may be from 200 to 700 mg.-hr., varied to suit the individual case. A platinum or gold screen seems best, a beta ray screen being used. Various mechanisms have been developed to hold the tubes in place. Green devised an ingenious apparatus with multiple movable joints attached to a head clamp. If large amounts of element or radon are available, the time of exposure may be shortened to one or one and one-half hours, in which case manual retention may suffice. Gold implants of 1.0 or 2.0 mc. each are best imbedded in the large intralaryngeal masses. The seeds can be buried by means of a long curved trocar, using the indirect method. If the implants are kept 0.5 cm. away from cartilage, no untoward results need be feared. Cross-fire from both sides of the neck by means of deep external irradiation should supplement the internal irradiation in all instances. From 2 to 10 gm.-hr. may be given externally, using 1000 mg.-hr. per 2 sq. in. of skin area with beta ray screen at 1 inch distance as a standard. Intense irradiation with an applicator containing from 1 to 4 gm. of radium, at 6, 10 or 15 cm. distance over the lymphatics of the neck, probably gives the best prospect of favorable results.

Irradiation may be repeated in five or six weeks, keeping in mind reduced tolerance because of fibrosis and reduced blood supply. Extrinsic growths may be irradiated interstitially, using implants of radon or element needles, keeping 0.5 cm. from cartilage, and giving a dose of from 80 to 130 mg.-hr. per cubic centimeter of tissue. Here again deep external irradiation supplements the interstitial treatment, heavier when masses are extensive, but given even in the absence of metastasis. Palliative treatments are justified in advanced cases, external irradiation alone frequently causing considerable inhibition of growth and enlargement of the lumen, much to the patient's relief. Urgent cases occasionally require a laryngeal fissure, with the radium

packed within the cavity. Here the dosage may be increased, disregarding cartilage destruction in the hope of better palliation. Dosage over 1200 to 1500 mg.-hr. is almost certain to cause sloughing of the cartilage. Even where laryngectomy is determined upon, irradiation to the base of the wound by buried radium is indicated to deter recurrence. Necrosis of all malignant cells is the goal sought, but inhibition and encapsulation of cells in fibrous tissue slow the growth and permit the natural bodily resistance to lend its aid in combating the serious invasion.

Reaction. The general reactions are usually severe. Malaise, anorexia, headache, and occasionally nausea and vomiting follow heavy deep irradiations about this area, especially when more than 3 or 4 gm.-hr. are given. The reaction begins during the application and may last three or four weeks, according to the size of the dose and the duration and extent of the local reaction. When there is much destruction of tissue and consequent absorption, the general reaction is increased. In radium applications about the head, reactions seem to be more severe than from the same dosage applied elsewhere in the body. Free fluid intake and increased elimination lessen the reaction.

Locally, the reaction within the larynx begins within a few days when interstitial applications are made, and in five to seven or eight days when surface applications are made within the larynx. This reaction is characterized by swelling to the extent of local edema. This swelling may be marked if heavy irradiation is given. Such patients should be under close observation so that immediate measures can be taken should obstruction threaten. This swelling reaches its height about the end of the second week when surface applications are used, and a few days earlier when implants are buried. During the second and third weeks sloughing and absorption are in progress, and by the fourth or fifth weeks, healing is usually accomplished. When heavy external irradiation is given simultaneously with the intralaryngeal treatment the reaction is increased, both as to severity and duration. When possible, the external irradiation should precede the intralaryngeal application. Cough and expectoration ordinarily take care of any slough within the larynx.

Local measures, such as soothing sprays, sedatives, and local applications may be used to tide the patient over a troublesome period, but all manipulation should be gentle. Hemorrhage is rare with the dosage mentioned. End results, if good, are characterized by a pale membrane, scarred and shrunken; perhaps distortion of normal structures may occur from late contraction, but such changes may be negligible. Complete vocal recovery is rare. Extrinsic growths, if arrested, present fibrous thickening and shrunken masses about the original site. Repeated external irradiations in unsuccessful cases are justified, if only to prevent gross disfigurement and mutilating ulcers and defects.

Prognosis. The immediate prognosis is frequently good. All clinical evidence of growth may be eradicated, but unfortunately sooner or later recurrence usually takes place, either at the site of the lesion or in neighboring lymphatics. Extensive lesions may be controlled, and tracheotomy delayed, and the patient may come to his end by toxemia. Radium offers the best hope of cure if the cases are early, and the best means of palliation if they are extensive or advanced.

Case History

Mr. N. Aged fifty-five. Carcinoma of larynx. Loss in weight (50 lbs.); husky voice. Operated. Laryngofissure after tracheotomy. Curettement; 60 mg. of radium packed in larynx for twenty-four hours, with 0.5 mm. silver screen (1440 mg.-hr.) Also 2400 mg.-hr. with 100 mg. of radium at 1 inch distance, just lateral to the larynx on each side, with beta ray screen. Temporary improvement. Marked sloughing of all intrinsic cartilaginous surfaces. Died of disease, one year later.

References

Barajas, L. Radium treatment of laryngeal neoplasms. *Med. Ibera.* Special Number. I. *Cong. nac. de med. y cirug,* 101.

Callison, J. G. Histologic control of radium treatment in carcinoma of larynx. *Laryngoscope,* 32: 180, 1922.

Clerf, L. H. Laryngeal complications of irradiation. *Tr. Am. Laryng. Assoc.,* 49: 99, 1927.

Delavan, D. B. Radium in the field of laryngology. *Med. Rec.,* 90: 50, 1916.

Escat, E. and Laval, F. Laryngeal radium therapy by thyroid fenestration without surgical resection. *Ann. d. mal. d. l'oreille, larynx, etc.,* 43: 117, 1924.

Freer, O. T. Carcinoma of the larynx treated locally with radium emanation. *J. A. M. A.,* 79: 1602, 1922.

HARRIS, T. J. Radium in cancer of the larynx with particular reference to dosage and the dangers in its employment. *Laryngoscope*, 31: 872, 1921.
JACKSON, C. Cancer of the larynx. *Ann. Surg.*, 77: 1, 1923.
PFAHLER, G. E. Radiotherapy in carcinoma of the larynx with special reference to radium needles through the thyrohyoid membrane. *J. Radiol.*, 3: 511, 1922.
QUICK, D., and JOHNSON, F. M. Statistics and technique in the treatment of malignant neoplasms of the larynx, *Am. J. Roentgenol.*, N. S., 9: 599, 1923.
QUICK, D. Laryngeal cancer treated with radium. *Rev. espan de laringol, etc.*, 14: 68, 1923.

CARCINOMA OF THE ORBIT

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

PATHOLOGY. Carcinoma of the orbit is of the squamous-celled type, and ordinarily is an extension from epithelioma of the eyelids. Early in its course the growth pushes the eye forward and later the eyeball itself becomes involved. Vision is lost and the glands at the canthi become malignant. Corneal ulcer is a sequel, and when enucleation is done, the whole content of the orbit is often found to be a mass of malignant tissue.

RADIUM INDICATIONS. In cavities of this sort, radium is indicated on account of its property of destroying malignant tissue. When involvement is slight and extension is just beginning to take place, radium can often be inserted between the eyeball and the orbital wall to destroy the growth without damage to the normal function of the eye. When there is an extensive growth behind the eye, surgical removal of the eye together with the greater part of the malignant tissue is indicated, to be followed by radium which is well adapted to destroy what malignant tissue might be left behind and prevent recurrence in the site.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. If extension is beginning to involve the conjunctival fold and the subconjunctival tissues, two or three radium needles may be inserted backward between the eyeball and the bony wall of the orbit. Sixty to 70 mg.-hr. per needle are known to do no harm to the eye and such an

amount will frequently eradicate the lesion. The use of gold radon implants here is valuable. When the growth is extensive and enucleation is indicated because there has occurred loss of vision or loss of the hope of permanently eradicating the disease, radium is well suited to destroy malignancy in the base and prevent recurrence. The element, or radon, preferably with beta ray screen is packed within the cavity, either in tubes evenly distributed about the periphery or in a single tube centrally placed. From 1000 to 2500 mg.-hr. may be given, but caution is required to prevent necrosis of bone. Divided doses may be given, or a series of applications may be used. Deep external irradiation over the lids, attacking the lesion from the front, serves as cross-fire and aids in the prevention of extension or metastasis. One thousand milligram-hours at 1 inch distance with beta ray screen is an average dose, irradiating each 2 sq. in. once. The lids may be sacrificed, and one may even incur risk of loss of bone or late slough if there is hope of permanent cure. In hopeless cases, palliative treatment should be given and repeated when indicated, for nothing else approaches the value of radium for the amelioration of suffering in these cases.

Reaction. The reaction is usually marked when 2000 to 3000 mg.-hr. are given about the orbit. The proximity to the brain and the increased absorption augment and prolong the general reaction. Malaise, anorexia, vomiting and headache may continue for six to eight weeks, and there may occur real weakness and loss of weight.

Locally, the swelling is marked, and edema of the eyelids may occur, even to closing the eye. Pain is often severe. The whole content of the orbit may slough gradually or *en masse* by the fifth or sixth week. Repair and healing is slow because of the avascular nature of the field and because of the surgery or cauterization preceding the irradiation. Eight to ten weeks are required for the complete repair. Recurrences may be re-treated or it may be thought better to let the lesion alone. Free fluids and catharsis reduce the irradiation sickness and toxemia.

Prognosis. The prognosis is grave in the extensive cases but the conditions are urgent and radical treatment is justified. Early extensions can be arrested without damage

to the orbital contents. The primary focus must be cleared simultaneously. Extensions may be found growing backward into the orbit even after the primary growth has apparently disappeared.

Case History

Mr. M. Aged sixty-six. Carcinoma of orbit. Indurated, ulcerated hypertrophic lesion, site of inner canthus, right eye. Invasion of conjunctiva and orbital tissues mesial to eyeball. Sight lost years ago, due to old injury. Treated by 4.0 mc. radon in glass; i. e., 8 implants of 0.5 mc. each, placed homogeneously throughout involved tissue. Reaction severe followed by complete healing and quiescence. Died one year later of heart lesion.

References

Bell, G. H., and Tousey S. Non-operable tumor of the orbit and brow treated successfully with radium. *Arch. Ophth.*, 48: 531, 1919.

Shoemaker, W. T. Some observations on orbital growths: reports of three cases. *Penn. M. J.*, 26: 70, 1922.

Carcinoma of the Tonsil, Pharynx, and Nasopharynx

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. The lesions are ordinarily hypertrophic and of the squamous-celled type, raised and often pedunculated. In the nasopharynx, obstruction is often the first symptom. When found in the tonsil, carcinoma may resemble chronic inflammation, but early ulceration or the appearance of a friable, bleeding, fungating surface will soon arouse suspicion as to its malignant nature. Spread is by extension and early metastasis is uncommon. Enlarged cervical glands are occasionally the first indication of nasopharyngeal malignancy.

Radium Indications. Radium is strongly indicated in any malignant lesion about the tonsil, pharynx and nasopharynx. Surgical or thermoelectric measures result in incomplete destruction, necessitating radiation treatment of the malignant base. Later, accessibility to the lesion renders radium application possible. Careful application of radium or radon

requires a considerable degree of skill and dexterity, but not more than for the mechanical types of treatment. Destruction beyond the visible base is best accomplished by radium.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Interstitial applications are best, using gold implants containing 1.0 to 2.0 mc. or glass implants containing 0.5 mc. of radon per implant; but when implants are employed, the dose may consist of 1 implant per cubic centimeter of tissue. Element needles may be used though soft friable tissue and small lesions do not retain the needles well and implants are here indicated. In the case of low, flat or excavating lesions of the pharynx or nasopharynx, surface applications must be resorted to, employing screens allowing none or but a small percentage of the beta rays to pass. Especially in lesions of the nasopharynx is tubular application made necessary on account of inaccessibility for treatment, for to be successful complete vision is required for interstitial applications. In the nasopharynx the lesion may in many cases partly or completely surround a tube passed through the nose or upward from the pharynx. The mechanics of placing and retaining surface applicators requires ingenuity. In tonsil or pharyngeal lesions, the radium may be attached to long applicators which the patient may hold manually or with the teeth. Modeling compound, shaped to incorporate the tubes, may be held in place by the teeth. Other devices, such as tonsil clamps or head clamps with multiple joints, may be used to hold the radium against the lesion. Posterior nasal packs may occasionally be used or the radium on a semirigid applicator may be passed through the nares to the site of the lesion, and fixed externally to the nose. In any event, radium applied within the mouth or nose must be fixed on the outside or the applicator must be constructed in such a manner that it is impossible for the radium to be lost down the esophagus or trachea. This precaution is absolutely imperative.

When surface application must be used, treatment may be considered adequate in doses approximating 100 to 300 mg.-hr. per square inch of surface if a light screen is used, and

600 to 1000 mg.-hr. if a beta ray screen is employed. The treatments may be given in divided doses if they are more easily tolerated by the patient, or if only small amounts of radium are available. Local application of 0.5 per cent cocaine facilitates accurate application and accurate retention of the radium in place. Second applications or series may be started five to eight weeks later, if indicated. When using interstitial applications, vital structures and bone must be avoided by at least 0.5 cm., lest perforation of vital structure or bone necrosis result. When using a beta ray screen, the radium may be closer but caution is required and divided doses are probably safer. Caution in regard to bone may be disregarded but treatment must be done advisedly.

Irradiation of the deep lymphatics on both sides of the neck is indicated and should be done before the interstitial application when possible. If malignant masses are already present in the neck, heroic irradiation should be given. One thousand milligram-hours per 2 sq. in. of skin surface is safe at 1 inch distance, though it is subject to increase when skill and the amount of radium available permit. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10 or 15 cm. distance over the lymphatics of the neck probably gives the best promise of favorable results. Malignant masses persisting after six weeks should be irradiated again or irradiation may be combined with surgical excision.

Reaction. The general reaction consisting of malaise, anorexia, or even vomiting if heavy deep irradiation is used, comes on primarily during the application and for forty-eight to seventy-two hours afterward, and secondarily during the second and third weeks. Malaise may be the only complaint, or other symptoms may be present to a marked degree if there is much tissue destruction and absorption. Free fluid intake (40 to 50 ounces per twenty-four hours) and adequate bowel evacuation reduce the general reaction markedly.

Locally, the inflammatory reaction begins in three to six days and consists of swelling, redness and later sloughing. Dysphagia or nasal obstruction may be present, according to the location of the lesion. Pain in varying degrees is almost always noted. Sloughing becomes marked and

shrinkage of the lesion occurs during the third week, while subsidence of the inflammatory reaction and healing are accomplished during the fourth, fifth and sixth weeks, depending on the severity of the dosage and the extent of the lesion. Mouth washes are indicated. It may be helpful to use soothing sprays, or even swabbing of the parts with local anesthetics, such as butyn, cocaine or the like, but all manipulations must be gentle. Fluids and adequate nourishment must be kept up lest the patient lose weight and consequent power of recuperation and resistance. Complete necrosis of all malignant tissue is sought. Puckering and retraction of the mucous membrane, pale and smooth, result. The "feel" is that of hard rubber, which is sometimes difficult to distinguish from the induration of incomplete destruction or recurrence. Ulceration, increase in size of the scarred mass, or extension of induration to adjacent tissues, indicate recurrence or failure of complete destruction. The patient must be kept under close observation.

Prognosis. In the majority of cases the ultimate outcome is recurrence, though survival for many months or even years is not uncommon. If complete local destruction and healing cannot be accomplished, or if lymphatic metastases persist, heroic measures must be instituted or palliative treatment only attempted. Early lesions with no evident extensions can often be irradiated, and months or years may elapse before local recurrences or extensions appear. Extensive or advanced cases are best palliated by radium. Frequently at the very outset, the problem of palliation or attempted eradication must be faced and solved, in order that suitable treatment may be instituted. When palliation only is sought, the character and end results of the treatment must be weighed carefully over against what the probable course would be if nothing were done. The radiologist should be sure that, all things considered, radium treatment is better than no treatment at all. It must be remembered, too, that palliative radium treatments frequently succeed far beyond expectation and that predictions made are often not borne out by the facts. Every individual lesion reacts in its own way and only treatment will demonstrate whether the reaction will be favorable.

Case Histories

Mr. L. Aged seventy-three. Carcinoma, soft palate. Flat, raised, ulcerated, firm lesion, 3 cm. diameter, 0.5 cm. thick, middle anterior surface soft palate, present for six months. Biopsy. Treated by 2.0 mc. radon in 0.5 mc. glass implants. Reaction severe. Destruction of soft palate. Recurrence in six months in three areas, one anterior and two at right of original site. Treated by 1.0 mc. radon gold implants in each of two lesions and two implants in third. Incomplete destruction of lesion on palate. Lesion now quiescent for six months. No enlarged glands in neck. Well for twenty-two months.

Mrs. O. Aged sixty. Carcinoma, tonsil. Indurated, ulcerated swelling, left tonsil, present six months. Enlarged indurated glands, left side neck. Cauterization of tonsil done previous to irradiation. Treated by 3300 mg.-hr. radium, left side of neck at 1 inch distance, over three areas, beta ray screen. Also 1100 mg.-hr., same technic, right side neck. Three weeks later 2.7 mc. radon in 5 glass implants in tonsil lesion. Clinically well eighteen months.

References

Armstrong, M. Tumors involving the oral cavity, upper respiratory passages, and ears, and some observations following the use of radium. *J. Iowa M. Soc.*, 12: 187, 1922.

Brindel. A case of malignant tumors of the nasal fossa and of the maxillary sinus treated with radium. *Rev. de laryngol. etc.*, 43: 726, 1922.

Roy, D. Case of intranasal epithelioma cured by excision and radium. *Ann. Otol., Rhinol. & Laryngol.*, 30: 748, 1921.

Collet, F. J. Radium therapy of the pharynx and the esophagus. *Arch. internat. de Laryngol., etc.*, 29: 705, 1923.

Constantin, P. M., and Dupeyrac, G. Cancer of the palate and soft palate. *Bull. d'oto-rhino-laryngol.*, N. S. 20: 15, 1922.

Corbett, J. J. Radium clinic for treatment of eye, ear, nose and throat conditions. *Boston M. & S. J.*, 190: 1082, 1924.

Crowe, S. J., and Baylor, J. W. Benign and malignant growths of the nasopharnx and their treatment with radium. *Arch. Surg.*, 6: 429, 1923.

Grier, G. W. Deep roentgen and radium therapy in carcinoma of the tonsil. *Am. J. Roentgenol.*, 11: 537, 1924.

Keith, D. Y., and Keith, J. P. Juvenile nasopharyngeal fibroma treated with radium. *Kentucky M. J.*, 23: 26, 1925.

Lane, L. A. Radium in benign conditions of the nose and throat. *Minnesota Med.*, 7: 578, 1924.

Lannois, Sargnon and Moutet. Radium treatment of tumors in otorhinolaryngology. *Bull. Acad. de Méd.*, Paris, 3. S., 81: 638, 1919.

Lenormant C. Carcinoma of the tonsil. *Bull. et mém. Soc. de Chir. de Paris*, 48: 1209, 1922.

Martinez, E. Otorhinolaryngologie cases treated by radium. *Rev. méd. cubana*, 33: 100, 1922.

Mazzoni, L. X-ray and radium treatment of scleroma of the nasopharynx. *Radiol. med.*, 10: 53, 1923.

New, G. B., and Figi, F. A. Treatment of fibromas of the nasopharynx. *Ann. Otol. Rhinol. & Laryngol.*, 34: 191, 1925.

Pancoast, H. K. Malignant disease of the throat and sinuses. *J. A. M. A.*, 69: 980, 1917.

Pinch, A. E. H. Carcinoma of the palate. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 52, 1923.

Pinch, A. E. H. Malignant growths of the pharynx. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S. 2: 54, 1923.

Pinch, A. E. H. Innocent tumors of the pharynx. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 54, 1923

Pinch, A. E. H. Epithelioma of the tonsil. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 53, 1923.

Quick, D. Treatment of malignant neoplasms of the tonsils. *J. Radiol.*, 3: 173, 1922.

Ranson, J. R. Radium in the treatment of malignant tumors of the nose and throat. *Laryngoscope*, 33: 883, 1923.

Robinson, G. A. Radium treatment of neoplasms of the upper air-passages. *J. A. M. A.*, 84: 248, 1925.

Salinger, S. Radon therapy in carcinoma of the mouth and throat. *Arch. Physical Therapy*, 8: 279, 1927.

Sargnon. Malignant neoplasms of the pharynx and larynx. *Arch. internat. de laryngol., etc.*, 29: 972, 1923.

Schele, A. An apparatus for the facilitation of radium treatment in the mouth and pharynx. *Acta radiol.*, 1: 540, 1922.

Sonnenschein, R. Radium in the treatment of malignant tumors of the nose and throat *J. A. M. A.*, 75: 860, 1920.

Stevens, R. H. Malignant growths of the paranasal sinuses treated by irradiation. *Am. J. Roentgenol.*, 11: 532, 1924.

Tonsils (chronically hypertrophied and infected)

Diagnosis is not discussed in this outline but should be established by careful examination in every instance. (See p. 13.)

Pathology. Chronically infected tonsils are usually hypertrophied. The enlargement is due to an increase in lymphoid tissue, enlargement and engorgement of the tonsillar crypts, and general chronic inflammatory swelling. The tonsil may be giving rise to symptoms mechanically, it may be the cause of sore throat, and it may be harboring retained mucopurulent material in the crypts, resulting in the absorption of toxic material and bacteria into the general circulation,

thus acting as a port of entry for the various pyogenic organisms. Lymphatic nodes in the draining lymphatic chain may be chronically enlarged, due to absorption from the diseased tonsil.

Radium Indications. The lymphoid tissue in chronic hypertrophic tonsils is especially susceptible to the beta and gamma rays of radium. Complete or partial atrophy of the lymphatic tissue in these organs has repeatedly been brought about by radium rays. The atrophy resembles, to a marked degree, senile atrophy and is accompanied by a decrease in the inflammatory processes, much the same as occurs in middle and late adult life.

In general, the surgical removal of tonsils is considered the treatment of choice. It is probably better to remove foci of infection rather than to lock them up in fibrous tissue.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Surface and interstitial radium applications are chiefly employed in the treatment of infected tonsils. Deep external irradiation may also be used. Unscreened, flat or concave applicators containing 10 to 30 mg. covered only with rubber may be placed in contact with each tonsil for one or two hours, the application being repeated in four to six weeks, or earlier in the smaller doses, if necessary. Swabbing the mucous membrane with cocaine solution suffices for anesthesia. Flat or tubal applicators, screened to transmit 10 to 15 per cent of the beta rays, may be employed against the mucous membrane of the tonsils in dosages of 30 to 100 mg.-hr. per tonsil, in single or divided doses, from two to four weeks apart, the treatment being continued according to the degree of atrophy and symptomatic improvement in the condition. One or two metal needles, delivering 10 to 15 per cent of the beta rays, may be inserted into the tonsil parenchyma, delivering 30 to 50 mg.-hr. per tonsil; or gold implants of 1.0 to 1.5 mc. may be introduced, one for each cubic centimeter of tissue. One such exposure frequently results in therapeutic atrophy. Deep external irradiation over the tonsil area with dosage from 300 to 1200 mg.-hr., at distances of ½ to 1 inch, with beta ray screen, according to

the milligram-hour dosage, has been employed successfully in infected tonsils. In general, if given in fractional form, treatments are repeated at intervals of two to four weeks, until the therapeutic results are obtained. Single, accurately estimated applications, properly applied, may be perfected with continued experience, and adjusted to the size of the tonsil and the age of the patient, the smaller dosage being sufficient in smaller tonsils and younger patients.

Reaction. A general reaction is mild or absent. Locally the reaction to unscreened radium begins within a few days as an inflammatory surface reaction with superficial white membranous exudates. Some swelling occurs in the tonsil. By the end of the second or third week the exudate has disappeared and shrinkage is marked or slight, according to the dose, and the susceptibility of the tonsillar tissue. Second applications are then indicated if atrophy is not sufficient. Second reactions resemble the first. Occasionally third applications are required. Interstitial insertion results in a diffuse swelling of the tonsil within a few days without marked surface changes. The inflammatory swelling subsides during the second week with marked atrophy of lymphoid tissue, followed by continued shrinkage for from three to six weeks or longer. The lymph follicles may be almost completely atrophied, with some fibrous tissue replacement and much shrinkage. The crypts are emptied and the surface of the tonsil presents a smooth, pale membrane. In favorable cases, the tonsil atrophies to normal or even to a senile atrophic condition. Improvement in symptoms, due to toxic absorption, usually begins within a few days. Bacterial exudates decrease in amount and virulence. Locally and generally the condition is relieved in four to six weeks in favorable cases. Unfavorable cases may be very resistant but generally there is practically complete local atrophy. Deep external irradiation should not cause a local inflammatory reaction but only a gradual shrinkage of the susceptible lymphoid tonsillar tissue. Rarely there is an aggravation of symptoms, such as arthritis, glandular swelling or neuralgic pains, following radium treatment. General improvement may be slight. Local recurrences of inflammation and hypertrophy occur rarely.

PROGNOSIS. Radium treatment of chronic, infected hypertrophied tonsils is appropriate with a high proportion of ultimately successful results. However, it seems inadvisable to supplant tonsillectomy by radium treatment; rather should radium be reserved for cases unsuitable for surgery because of temperamental conditions, general or local contraindications to anesthesia or some other special consideration, which influences one to refrain from surgical excision.

REFERENCES

BERVEN, E. Radiological treatment of chronic tonsillitis. *Acta Radiol.*, 2: 301, 1923.

GUARINI, C. Radiological treatment of chronic tonsillitis and hypertrophy of the tonsils. *Riforma med.*, 41: 252, 1925.

ISRAEL, S. X-ray treatment of tonsils and adenoids, a preliminary report. *Texas State J. M.*, 18: 301, 1922.

LANE, L. A. A study of the tonsil question with a preliminary report of roentgen ray and radium therapy in the treatment of pathologic tonsils. *Minnesota Med.*, 6: 97, 1923.

MOYER, C. C. Radium and lymphoid tissue. *J. Ophth., Otol. & Laryngol.*, 28: 432, 1924.

ROBINSON, C. F. Radium treatment of diseased tonsils. *Am. J. Roentgenol.*, 9: 588, 1922.

SIMPSON, C. A. Atrophy of lymphatic and tonsillar tissue by radium and x-ray. *Virginia M. Monthly;* 48: 473, 1921. *J. Radiol.* 2: 35, 1921.

SIMPSON, C. A. Radium treatment of tonsils. *Am. J. Roentgenol.*, 12: 527, 1924.

WELLS, W. A. On the practicability of effecting a complete atrophy of the tonsils by the use of radium. *Southern M. J.*, 14: 907, 1921.

WELLS, W. A. On the use of radium to induce atrophy of the faucial tonsils—histologic evidence. *Laryngoscope*, 33: 681, 1923.

WILLIAMS, F. H. The treatment of tonsils by radiations from radium salts instead of operation. *Boston M. & S. J.*, 187: 412, 1922.

WILLIAMS, F. H. Treatment of tonsillar hypertrophy by radium therapy. *Paris méd.*, 13: 110, 1923.

WILLIAMS, F. H. Prompt action of radium radiations in the treatment of small or large infected tonsils and lingual tonsils. *Boston M. & S. J.*, 188: 497, 1923.

WILLIAMS, F. H. The use of radium in the treatment of tonsils. *Am. J. M. Sc.*, 168: 18, 1924.

WITHERS, S. On the use of radium to effect an atrophy of pharyngeal lymphoid tissues. *Laryngoscope*, 32: 163, 1922.

SARCOMA OF THE TONSIL, NASOPHARYNX AND ORBIT

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance.(See p. 13.)

Pathology. While sarcoma of these structures is not common, it is rapidly progressive and destructive. Pressure and mechanical obstruction soon cause stenosis of the passage and destroy the function of the adjacent organs. Small round-celled and spindle-celled sarcomata are the more common forms developing from below the surface, rapidly enlarging and metastasizing early by the blood stream, probably more often than by the lymphatics. The tumor early distorts the organ and obstructs the air passages of the nose or throat, or in the case of orbital tumors displaces the eyeball forward. The sarcomatous process spreads by infiltration to adjacent soft parts. Ulceration with foul discharge is less common than in carcinoma. The degree of vascularity varies. Many types of cells may be found in varying proportions of connective tissue. Connective tissue in abundance is usually associated in an inverse proportion with rapidity of growth. Bone erosion and involvement follow in untreated cases.

Radium Indications. Radium is probably the method of choice in dealing with these rapidly growing, intensely malignant neoplasms. Radium rays when accurately applied are capable of readily destroying the malignant cells. Interstitial and deep external irradiation with maximum amounts of cross-fire yield results unattained by other methods. Postoperative interstitial irradiation combined with deep external treatment is indicated in surgical cases. The partial surgical removal of sarcoma probably hastens the progress and spread of the disease.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Interstitial applications give best results whenever completely accessible tumors are found. Element needles homogeneously placed, with a dosage of 100 to 130 mg.-hr. per cubic centimeter of malignant tissue, suffice for complete local destruction. Gold implants of 1.0 to 2.0 mc. per cubic centimeter of malignant tissue are effective. If interstitial treatment is mechanically impossible, surface irradiation should be resorted to.

From 100 to 130 mg.-hr. per square centimeter of surface will destroy all malignant tissue for a depth of 5 mm. Surgical removal, supplemented by interstitial irradiation in the depth of the wound, offers better results than surgical removal alone. The dosage of screened radium in the depth of a wound should not exceed 500 to 1000 mg.-hr. unless there is a cavity of a diameter of 4 or 5 cm., in which case the treatment is a cavity application. Such applications are best made at the time of operation. The orbit or the antrum will tolerate 2 gm.-hr. of unscreened radium within the cavity without extensive sloughing or bone destruction.

Deep external irradiation over the adjacent skin area is an integral part of the treatment and should be given at the same time. The maximum dosage tolerated by the skin should be applied as rapidly as possible. One thousand to 1200 mg.-hr. of gamma rays at 1 inch distance may safely be used over each 2 sq. in. of skin area. Intense irradiation with an applicator containing from 1 to 4 gm. at 6, 10, or 15 cm. distance probably gives the best promise of success. Repetition may be given in four weeks if the initial skin reaction is mild. The fact that almost invariably there are malignant cells beyond the clinical margin of the disease requires deep external heavy irradiaton in every instance. Repetition of skin dosage is ordinarily limited only by the skin reaction. Interstitial or surface applications are best repeated when there is clinical evidence of incomplete destruction or of recurrence of malignant growths.

Reaction. The general reaction is usually severe when heavy external irradiation is applied about the head. The reaction begins at the time of application and continues for several weeks, being greater during the third week, especially when there is extensive tissue destruction and absorption following interstitial irradiation. Malaise, nausea, headache, anorexia, vomiting and pain are all apt to be pronounced. Loss of weight and lowered blood count are frequent complications. Convalescence may be slow, for the patient is severely ill. Supportive measures are indicated. The patient must be nourished and supplied with plenty of fluids, and elimination must be promoted. Blood transfusion preliminary to, during, or after

the treatment, may be indicated in many cases. Many of the patients are young, and all effort should be made to promote general bodily health and resistance to combat the disease as well as to support the treatment.

Locally the reaction begins within a few days. So susceptible are some sarcomata to radiation that the preliminary inflammatory swelling is almost absent. Decrease in size of the mass may be noted within a few days, and shrinkage may continue until within three weeks the tumor may practically disappear. The more cellular types of tumor yield rapidly. When the fibrous elements predominate, the tumors may shrink but little and thus seem not to yield to the treatment. When the interstitial treatment is used disintegration and absorption are usually complete by the fourth week. Surface irradiations with gamma rays yield results more gradually. Deep external irradiation may not accomplish reduction in size of the mass until the third or fourth week. If there is no reduction in the size of the mass by the fifth week one of three conditions usually obtains: (1) The tumor cells are resistant, (2) the fibrous framework predominates, or (3) regrowth is already in progress.

Complications arise from hemorrhage due to eroded vessels from the caustic action of the beta rays in interstitial application. Extensive sloughing *en masse* may occur from heavy interstitial irradiation. Bone destruction may occur when radium is placed too close to bone or from the destruction of the malignant tissue which had already invaded the bone when treatment was instituted. Pain may be severe, due to swelling or proximity of the lesion to nerve trunks, or subsequently because of fibrous tissue contraction. Late fibrous tissue contraction may result in sloughs several months after treatment. Intractable ulceration may follow extensive tissue destruction. Eventually these ulcerations heal if the disease has been eradicated locally. Analgesics, mouth washes, mild antiseptics, irrigations, and often opiates are required to tide the patient over the severe local reactions.

General health must be conserved and sleep must be procured if the disease is to be controlled. In successful cases the tumor mass shrinks to a minimum and remains quiescent. Ulceration, if present, heals. Pain and pressure are relieved.

Secondary masses or extensions diminish beyond observation and remain quiet. In a small percentage of cases, months and years may elapse before there is evidence of regrowth. In the average case local recurrence or extensions begin to appear within a few weeks and re-treatment is indicated but again the same faulty result is secured, and the general condition of the patient fails rapidly or slowly, according to the extent of the lesion or the reaction to treatment. Too often the benefits of palliative treatment are outweighed by the discomforts and suffering due to further irradiation. A fatal termination is frequently delayed but seldom avoided.

PROGNOSIS. Sarcoma about the mouth, orbit and face presents an unfavorable prognosis. Attempts should be made to eradicate the lesion but with the most guarded prognosis. There seems to be little doubt that radium offers the best hope of cure and is probably the best agent of palliation in these cases.

CASE HISTORY

Mr. S. Aged fifty-five. Angiosarcoma of nasopharynx. Soft, bleeding, obstructing mass, left lateral nasal wall behind soft palate. Destroyed by diathermy one week previous to irradiation. Biopsy. Treated by 800 mc.-hr. with 100 mc. of radon, with a beta ray screen, against lesion. Repeated in one month. No recurrence at site. Headaches after one year.

REFERENCES

BOGGS, R. H. Radium and deep therapy in the treatment of malignancy (sarcoma of the tonsil and throat). *Radium*, 18: 58, 1922.

GLASSMAN, I. Adenosarcoma of the right tonsil cured by radium emanation seeds. *M. J. & Rec.*, 121: 86, 1925.

PINCH, A. E. H. Sarcoma of the jaws. A report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 47, 1923.

PINCH, A. E. H. Sareoma of the palate. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 52, 1923.

PINCH, A. E. H. Sarcoma of the tonsil. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 53, 1923.

STEIN, O. J. Case of nasal sarcoma cured by radium. *Ann. Otol. Rhinol. & Laryngol.*, 26: 782, 1917.

WOODMAN, E. M. Sarcoma of nose cured by radium. *Eye, Ear, Nose & Throat Monthly*, 2. 375, 1923.

PART V

MISCELLANEOUS AND SKIN LESIONS

MISCELLANEOUS AND SKIN LESIONS

Trachoma

Encouraged by the results obtained with soft radium rays in vernal catarrh, a chronic resistant granular condition in the tarsal conjunctiva, an effort has been made to treat trachoma. Varying degrees of success have attended the effort. The longer exposure required for this resistant condition results in a more marked local reaction. While the results are encouraging, the treatment is not curative in a large proportion of cases. Further experience may achieve more satisfactory results in the treatment of trachoma with soft radium rays. (See also Vernal Conjunctivitis, below.)

Reference

Müller, L., and Högler, F. The cure of trachoma by radium. *Wien. klin. Wchnschr.*, 35: 954, 1922.

Vernal Conjunctivitis

Diagnosis is not discussed in this outline but should be established by every possible means. (See p. 13.)

Pathology. This lesion is a chronic proliferation of the tissues of the conjunctiva, subject to annual exacerbations. Local granulations are present, consisting of thickened epithelial and fibrous tissue. The hard granulations are commonly the site of hyaline degeneration. Rarely the ocular conjunctiva is involved.

Radium Indications. The soft rays from radium have been used repeatedly with success in clearing up this very troublesome condition. The property of the rays to substitute fine for heavy fibrous tissue and to inhibit epithelial proliferation and hypertrophy are the active factors in the treatment of vernal conjuctivitis. Local leucocytosis and local transient congestion may also encourage the curative process. Heavy dosage should be avoided, especially to the ocular conjunctiva, for it may result in corneal or lenticular opacities.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The surface application of unscreened radium homogeneously applied over the involved surface under cocaine anesthesia, is the method commonly employed, using from 10 to 50 mg. of radium, evenly distributed over the surface in a special applicator or in tubes kept constantly moving to prevent over-irradiations and consequent slough of any area. The dosage varies from 10 mg. of unscreened radium for five to ten minutes over each lid to 50 mg., screened with 0.5 mm. of aluminum, for thirty minutes (the latter constituting heroic dosage) in markedly thickened, chronic and resistant cases. Full strength flat applicators or 10 to 25 mg. glass tubes of element or radon may be used directly against the conjunctiva, keeping the applicator in motion or moving it at three to five minute intervals to prevent overexposure. Small dosage is preferable at the outset, repeating from two to four weeks later, depending upon the reaction and results of the previous treatment.

Reaction. There is no general reaction. Mild, local inflammation begins within five days, characterized by injection, increased lacrimation, and discharge with pain, burning, or only mild discomfort. By the tenth to the fourteenth day the inflammatory reaction begins to subside, with resulting shrinkage of the granulations, or, in favorable cases, their complete disappearance. At the end of four weeks the reaction has usually subsided so that end results may be estimated. Favorable cases are cleared up. Unfavorable cases require further treatment in repeated or increased dosage. Carefully adjusted, second or third applications result in clinical cure in most cases. Dense, heavy resistant granulations may require heavier dosage and then, as in all instances, the radium should be kept as far as possible from the eyeball by lid retraction and by screening the soft rays on the side of the applicator toward the eye. No absolute contraindications exist, but the danger of injury to the cornea and lens must be reckoned with at the outset. Recurrence may appear the next year or later. One treatment then usually clears up the condition.

PROGNOSIS. Practically all cases of vernal conjunctivitis yield to careful radium treatment in from one to three exposures. Recurrences yield even more readily. The value of radium in this troublesome condition is frequently overlooked.

REFERENCES

NARIN AMAT, M. A severe tarsal form of vernal conjunctivitis cured with radium. *Siglo med.*, 71: 234, 1923.

HERNANDEZ, P. Vernal conjunctivitis treated with radium. *Arch. de oftal. hispano-am.*, Barcelona, 23: 388, 1923.

POSEY, W. C. Concerning vernal conjunctivitis. *Atlantic M. J.*, 27: 215, 1924.

SHUMWAY, E. A. Vernal conjunctivitis—its treatmcnt by application of radium. *Penn. M. J.*, 22: 793, 1919.

ACNE VULGARIS

Diagnosis is not discussed in this outline but should be confirmed in every possible manner. (See p. 13.)

PATHOLOGY. The lesions of acne vulgaris are characterized by local infections about hair follicles and sebaceous glands. The condition may be acute or chronic, and, if chronic, persistent. Scarring, fibrosis, keloidal formations and disfigurements are common characteristics. There is usually a general predisposition. It is a disease of young adult life, ordinarily occurring on the face, back, and chest.

RADIUM INDICATIONS. The beta rays of radium are suitable for the destruction of localized, small acneiform lesions. It is the alterative or local leucocytosis characteristic of the radium which hastens the involution of the process, inhibits scar formation and prevents recurrence to a small extent. The lesions are easy of access for treatment and observation and the applications are usually short. On account of the multiplicity of lesions roentgen-ray therapy is more commonly used.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. Full strength, glazed radium applicators are applied to the indurated lesions after the opening of any pustules which may be present. Windowed lead is used to

protect the normal surrounding skin. The dosage is kept under the vesiculation dose. From ten to thirty minutes with a screen of 0.1 mm. of lead and rubber for superficial lesions is a sufficient dose. From 0.1 to 0.5 mm. of lead and rubber with an exposure of between thirty to sixty minutes may be applied to deep-seated lesions of 3 mm. or more in depth. Applications may be repeated in three or four weeks. Areas in which the skin is completely involved may receive an erythema dose but not to the extent of vesicle formation. It would be well to begin the dosage below the erythema dose, and gradually to increase the exposure every ten or twelve days until the reaction within the lesion has reached the desired therapeutic degree.

Reaction. There is no general reaction. Locally, the reaction is characterized by an increased inflammatory process, rapidly progressing to crust formation or free drainage of the pustules. Drying and subsidence of inflammation follow to the stage of healing which is reached in ten to twenty days. Stab wounds are frequently necessary to open the pustules.

Prognosis. Radium is of great value in lesions resistant to all other types of local and general measures. Involution is hastened in the larger lesions; it is possible to shorten or abort incipient lesions. Recurrences are common. Scar formation is reduced to a minimum if one is careful to keep down the exposures so that ulceration will be avoided. Radium is of the most value in localized resistant cases.

Actinomycosis

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

This disease, common in cattle, rather rare in man, caused by the actinomyces bovis, a ray fungus, ordinarily begins by an involvement of the cheeks. "Lumpy jaw," as it is known in cattle, is derived from the hard, indurated swelling resulting from a marked increase in fibrous tissue, harboring within its interstices soft jelly-like masses made up chiefly of the fungus. Accessible areas, such as those of the mouth, gum, or cheek may be readily treated with radium. Favor-

able reports are found of cured cases by means of radium treatment, chiefly with the gamma rays, with doses amounting to several gram-hours. The inhibiting action of the rays upon the fungus or the alterative or local leucocytotic properties of the rays are probably the factors helpful in this disease. Inaccessible areas, such as the lung, stomach, intestines, or bone, probably can be only slightly affected by radium rays, except when employed in large quantities and with many gram-hours of dosage. Such applications require 1.0 to 2.0 grams, at 6 to 10 or more cm. distance.

Case History

Mr. Y. Aged twenty-four. Actinomycosis. Lesion measuring 2 by 1 cm., on skin of chest, discharging intermittently for three years. Biopsy. Discharging sinus present. Excised many times. Treatment: 2400 mg.-hr., with 100 mg., over two areas at 1 inch distance, using the beta ray screen. Three weeks later full strength plaques over ulcerated lesion for two hours, or 40 mg.-hr. Surface healed slowly at end of three months. Fluctuating swelling promptly appeared; broke through and organisms were recovered. Refused further treatment.

References

Heyerdahl, S. A. Actinomycosis treated with radium. *J. A. M. A.*, 73: 1928, 1919.

New, G. B. and Figi, F. A. Actinomycosis of the head and neck. *Surg., Gynec. & Obst.* 37: 617, 1923.

Angioma (rose spot, port-wine stain and cavernous angioma)

Diagnosis is not discussed in this outline, but should be established as thoroughly as possible in every instance. (See p. 13.)

Pathology. The dilated vessels composing these lesions are usually actually within the skin, rarely subcutaneous. Angiomata vary clinically according to the arrangement and number of dilated vessels. The rose spots contain numerous small capillaries and present a homogeneous surface. The port-wine stain or capillary angioma is less homogeneous in appearance, with some areas like the rose spot and other areas resembling the cavernous angioma. The surface is irregularly smooth, with raised zones here and there, and often contains many telangiectatic vessels. In cavernous lesions, which approach the character of erectile tissue,

there are large, irregular blood spaces communicating freely with each other. Their color is darker than the preceding two types. These lesions vary in size from 1 mm. in diameter to several centimeters. Angiomata are more commonly found about the face, head, neck, and arms. They are not neoplastic lesions. They may become the seat of skin dyscrasias; they may ulcerate or bleed spontaneously. The cavernous types increase in size early in life. They may become stationary during the second or third year of life. Later on in life the larger ones seriously affect the general blood supply to the parts. The colors of the three types described may be mentioned as rose, red, and purple in the order given.

Radium Indications. Both the beta and gamma rays of radium are capable of completely destroying these lesions by the mechanism of producing obliterative endarteritis. They are easy of access for treatment and observation. Contraindications are few; any skin dyscrasia which prevents treatment until cleared up is a contraindication.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Flat, full strength radium applicators, screened variously up to 0.1 mm. of lead, with rubber, may be used from five to fifteen minutes on the rose spot and the capillary lesion. The deeper the lesion, the greater should be the screening and slightly longer the duration of the application. Five to 10 per cent of beta rays may be safely employed at 3 to 5 mm. distance, giving as much as 5 mg.-hr. per centimeter. No visible skin reaction should be obtained in treating these superficial lesions. It is well to start with an application of a few minutes, and to increase the duration of the exposure up to a point just below skin tolerance. Three-week intervals are advised in order to allow time to observe the skin reaction if obtained. Deeper lesions extending 2.0 mm. or more into the skin require beta ray screening with the distance and dosage of gamma rays adjusted well below the erythema dose. From 200 to 300 mg.-hr. at 1 inch distance over each two square inches of skin surface is a safe application. Such treatments may be repeated every

four to six weeks and continued up to the practical disappearance of the lesion. The number of treatments depends upon the size and depth of the angioma, the limits probably being 10 to 18 treatments for the cavernous type. The earlier in life these treatments are begun, the better, since the cells lining these vessels are more susceptible during the first few months of life than later. Adults having cavernous angiomata require many times more radium and many more treatments, occasionally extending over a period of two or three years.

Reaction. There is no general reaction, and locally none should be visible. The superficial angiomata pale almost imperceptibly after six or eight months. It may require two years to accomplish the desired end result. One hundred per cent disappearance of the rose spot or port-wine stain is seldom attained. Cavernous types begin to shrink from the periphery, flatten from the top, and become paler within three or four months. Ten to eighteen months are required for complete disappearance. No scarring is present in successful cases. Pushing the treatment by increasing the dosage, lessening the screen, or shortening the period between treatments usually results in a local inflammatory reaction which is undesirable. This reaction may only be a scaling, but ulceration with crust formation and a subsequent flat scar surrounded by brownish pigmentation or telangiectasis is too often the sequel when a local inflammatory reaction is obtained. Complications are rare, erysipelas being one occasionally met with. Rose spots and capillary angiomata are rarely entirely eradicated. Cavernous lesions practically all disappear without trace when efficiently treated. There are no recurrences.

Prognosis. Rose spots and port-wine stains may be faded out to 70 per cent by careful beta ray treatment. Rose spots may be made unnoticeable under light cosmetics. Port-wine stains may be reduced to a point fully justifying the rather extensive treatment. Cavernous lesions in the very young can in practically all cases be completely eradicated without scarring. After these lesions have been present for many years, results are less certain, more difficult to obtain, requiring a greater number of treatments over a

prolonged period of time, and more frequently they involve the vital blood supply to important structures. In general these lesions are very satisfactorily treated with radium and the end results are gratifying in practically all cases.

Case History

Baby D. Aged nine months. Hemangioma. Raised red, puffy, compressible lesion close to hair line on forehead, 1 by 0.7 cm. Six treatments one month apart at 1 inch distance using beta ray screen with average of 150 mg.-hr. per treatment. Lesion disappeared in nine months. No scar or sign of lesion visible.

References

Abbe, R. Lymphangioma and radium. *Med. Rec.*, 88: 215, 1915.

Aikins, W. H. B., and Harrison, F. C. A case of nævus linearis treated by radium. *Urol. & Cutan. Rev.*, 27: 212, 1923.

Beck, A. Radium treatment of hemangiomas. *München. med. Wchnschr.*, 68: 1248, 1921.

Jones, A. C. A case of orbital hemangioma treated with radium. *Northwest Med.*, 24: 11, 1925.

Kummer, L. Radium treatment of angiomas of the skin. *Strahlentherapie*, 15: 506, 1923.

Laborde, S. Radium therapy of vascular nevi. *Progrès. méd.*, 36: 531, 1921.

MacKay, H. Nevi and their treatment by radium. *Canad. M. A. J.*, 14: 394, 1924.

Morrow, H., and Taussig, L. R. Radium therapy of vascular nevi. *Am. J. Roentgenol.*, 10: 867, 1923.

Newcomet, W. S. The treatment of nevi. *Am. J. Roentgenol.*, 4: 605, 1917.

Novak, F. A. Jr., and Cottle, M. H. Angiomata of the larynx. *Eye, Ear, Nose & Throat Monthly*, 1: 565, 1923.

Pinch, A. E. H. Treatment of cavernous naevi of the lips. A Report of the Work at the Radium Institute, London, Jan. 1, 1922 to Dec. 31, 1922. *Radium*, N. S., 2: 44, 1923.

Quigley, D. T. Preliminary report of a large angiomatous tumor in baby, treated by radium. *Western Med. Rev.*, 20: 235, 1915.

Rulison, R. H., and McLean, S. The treatment of vascular nevi with radium. *Am. J. Dis. Child.*, 25: 359, 1923.

Simpson, F. E. Radium in the treatment of vascular nevi. *Surg. Gynec. & Obst.*, 38: 407, 1924.

Simpson, F. E., and Flesher, R. E. Radium in the treatment of vascular nevi. *J. A. M. A.*, 89: 2028, 1927.

Swanberg, H. Nevus vasculosus (strawberry mark); report of a case cured by radium therapy. *J. Radiol.*, 4: 284, 1923.

Swanson, C. Removal of angiomas with radium *J. M. A. Georgia*, 12: 181, 1923.

Blastomycosis

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Blastomycosis is a chronic inflammatory process of the skin and subcutaneous tissue caused by the yeast-like blastomyces. The organisms are found in encapsulated hyaline globules which set up mild chronic inflammatory processes in the surrounding connective tissue with endothelial proliferation and leucocytic infiltration. Necrosis and breaking-down of these globules results in ulcerated crusting lesion, hypertrophic in character. There is a spontaneous tendency to heal. The disease usually remains localized. It spreads in some areas and heals in others; the lesions rarely become generalized.

Radium Indications. According to reports, soft beta and gamma rays have been successfully employed to clear up blastomycosis in a small number of cases. The alterative and necrosing properties of the rays are probably responsible for the reported improvement in this disease.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Radium, unscreened or but lightly screened, serves best in the treatment of blastomycosis. Slightly raised lesions having a thickness of less than two or three millimeters are satisfactorily treated by full strength plaque applicators with exposure of thirty to sixty minutes per area. When the lesions are raised to several millimeters, screens intercepting from 60 to 90 per cent of the beta ray permit longer exposures, affecting the deeper layers without complete caustic necrosis of the first two or three millimeters. With this technic, the dosage may be increased to between 15 and 30 mg.-hr. per square centimeter of surface. Occasionally it may be advisable to use gamma rays only as preliminary irradiation in deep-seated lesions. From 50 to 75 mg.-hr. per square centimeter of surface may be applied with satisfactory results in the deep tissues. Treatment may be repeated at intervals of four to eight weeks, depending upon the severity of the reaction, its duration and the results

of the previous treatment. Three or more applications may be necessary to accomplish complete eradication.

Reaction. The general reaction is slight or absent. Locally, the inflammatory reaction begins within a few days. Degeneration, distintegration, liquefaction, absorption, or exudation and crust formation follow in order named during the first twenty days. Crusts separate or become desiccated by the third or fourth week, at which time observations can be made as to healing, extension, recurrence, and missed or under-irradiated parts. Only slight pain or discomfort results locally. Re-treatment is accompanied by much the same reaction. Complications are few, pyogenic infection being the one most likely to occur. Favorable cases terminate after two or three treatments with a pale, depressed tissue paper-like scar free from crusts or hypertrophic areas. Unfavorable cases destroy deeper structures or involve them to such an extent that repair is protracted. Few cases carefully irradiated fail to yield unless they are very extensive, with serious involvement of deep-lying tissues. Recurrences may appear if the lesions were extensive or multiple.

Prognosis. Radium treatment probably offers the best method for temporarily as well as for permanently relieving this rather rare but troublesome and disfiguring disease.

Reference

Simpson, F. E. Radium in the treatment of blastomycosis. *J. A. M. A.*, 62: 844, 1914.

Cicatrices (scars)

Diagnosis is not discussed in this outline but should be established as accurately as possible in every instance. (See p. 13.)

Pathology. These lesions are characterized by fibrosclerotic bands with or without keloidal tissue. They commonly follow burns, wounds, luetic ulcers, scrofula, and by their contraction result in deformities and disfigurements which limit function. Ordinarily the deformity increases with the lapse of time.

Radium Indications. The beta or gamma rays of radium are capable of reducing these sclerotic bands and causing them to be replaced by a fine, pliable fibrous tissue network.

They are easy of access for observation or treatment. Ordinarily they are not painful. It is not necessary to cause a physical reaction and there are no contraindications to radium therapy in these cases. The results are not always sure but in the more severe instances the use of radium is well worth while.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. In general, the beta ray screen is employed at some distance from the lesion. One thousand milligram-hours at 1 inch distance over each 2 sq. in. of surface, or 300 mg.-hr. at ½ inch distance should be an adequate dosage, which may be repeated at intervals of six or eight weeks. If the scar is linear or irregular in shape, the adjacent skin should be protected by a sheet of lead, with a window cut in it to fit the lesion. The beta rays may be used on small lesions, seeking to employ the caustic action of the ray. A screen of 0.1 mm. of lead should be used, and rubber to reduce telangiectasis and pigmentation as much as possible. Small lesions ordinarily require one treatment, which may be repeated in two months, if the dosage was insufficient or portions were missed. The caustic method should be employed only when satisfactory results can be obtained in one or two treatments, otherwise the slower gamma ray method is advisable.

Reaction. There should be no general reaction. If the gamma ray method is employed, no visible erythema occurs. A very gradual softening and shrinking with increased pliability and leveling of the mass continues for months up to two years. The local reaction, if the caustic method is employed, begins within a few days as an inflammatory redness, with the formation of moisture and crusting, and, finally, drying and separation of the crust at the end of six or eight weeks. In this instance in the end result there is a soft white, pliable, often depressed scar, with occasional telangiectasis and slight pigmentation. Even with these the end result is far superior to the original lesion.

Prognosis. Radium cannot be regularly depended upon to remove vicious scars. If the scar includes considerable

keloidal tissue there is more likelihood of a good result, for the rays seem to have a more or less specific action upon it. Even in its absence a softer, more elastic scar results after adequate radium treatment. The contracture is relieved, the limited motion lessened, and a fair proportion of the cases are markedly improved. Radium should be employed in an attempt to relieve the deformity and limited function caused by cicatrices of the severer types.

Case History

Miss B. Aged seven. Cicatrix. Burn from hot water involving posterior aspect, right leg, from middle of calf to middle of thigh. Average width 5 cm. Thick hypertrophic scar, with contraction preventing extension of leg. Lesion 0.7 to 1.0 cm. thick. Treated by 10,000 mg.-hr. at 1 inch distance, averaging about 500 mg.-hr. to each 2 sq. in. of area. The total was divided into four treatments about sixty days apart. Extension of leg at sixty days. After one year, a soft pliable scar 2 to 3 mm. in thickness with no ulceration or limitation of motion. No fissures. Element of keloid in this lesion.

Chronic Eczema

Diagnosis is not discussed in this outline but should be established as accurately as possible in every instance. (See p. 13.)

Pathology. Eczema is a rather ill-defined skin lesion, deeper than an erythema, characterized by moisture or weeping, unlimited in extent and duration. Secondary papules, pustules, and crusts are not uncommon. Itching is usually present. Occasionally the lesions heal with atrophy, or a thickened fibrous skin. The sites are various. In general, eczema is a type of chronic dermatitis.

Radium Indications. Beta rays from radium are suitable for the cure of the lesions by their alterative action. The lesions are of easy access for treatment and observation. Extensive areas not easily covered with a few plaques are commonly treated with roentgen rays. The amount of irradiation needed is small. Acute inflammatory processes should be cleared up before treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The soft beta rays from unscreened, full strength glazed plaques, covered only with rubber, may be applied from one to two minutes as an initial dose. Exposures may be gradually increased in intervals of from seven to ten days, in order to determine the therapeutic dose and individual tolerance. Each area involved should be completely covered, as well as a zone extending 1.0 to 2.0 mm. beyond the margin. In general, the dosage should be adjusted to the case, carefully avoiding any acute inflammatory reaction. Needles or tubes may be used in lieu of plaques but the soft beta rays which are so valuable are screened out by the walls of the needles. The bare glass capsule may be used by keeping it in constant motion over the lesions until the proper amount of homogeneous radiation has been given. The therapeutic dose is well below the erythema dose. The presence of a crust indicates the need of greater distance from the radium to the depth of the lesion, which will increase the time of exposure correspondingly. Gradually increasing doses are repeated until the therapeutic effect is reached. Repeated applications may be made in fifteen to twenty days to irradiate missed areas or to supplement insufficient previous irradiation.

Reaction. There is no general reaction. Locally, there is a slight inflammatory reaction within three to five days. As a rule, the itching is reduced within thirty-six hours. The reaction is transient, followed by drying, crusting or scale formation, and is followed rapidly by decreasing redness and subsiding inflammation of the skin. Healing is usually accomplished in from ten to twenty days. If the reaction is marked by ulceration and if deep crust formation inadvertently occurs, the duration of the reaction and the healing may be delayed and scarring may result. Favorable cases terminate with the disappearance of the lesion and only such scarring as the disease may have produced. Recurrences are not uncommon but these should yield promptly to further radium treatment.

Prognosis. Resistant, chronic eczema yields in the majority of instances to a short exposure of an efficient soft beta radiation. Very extensive areas are tedious to treat but the radium treatment is available, and usually reliable.

Case History

Mr. B. Aged forty. Eczema. Flat, slightly reddened, scaling area 2.0 by 1.5 cm., located 3.0 cm. from anus. Present many years. Some weeping at times. Itching. No induration. Treated by 12.5 mg. needles, 1 cm. apart, with 0.7 mm. rubber placed against lesion for thirty minutes, at intervals of about two months, for five applications. Relief from symptoms. Thirteen per cent of beta rays employed. Some slight scarring with telangiectasis of mild degree. Well for two years.

References

Montgomery, D. W., and Culver, G. D. Eczema of the vermilion border of the lips. *Med. Rec.*, 98: 141, 1920.

Sakdabolraksh, P. Treatment of eczema by radium. *Siamese Red Cross M. J.*, Bangkok, 3: No. 2, 1920. Abs. in *J. A. M. A.*, 76: 1046, 1921.

Deafness

Various reporters have claimed improvement in hearing, irrespective of the pathologic basis of the condition, from radium treatment. Various applications of gamma rays have been made in and around the external auditory canal with recorded degrees of improvement in hearing. The alterative property of the rays or perhaps the replacement of coarse fibrous tissue by fine pliable strands in conditions of chronic inflammatory changes may have some bearing on the result obtained. Results, such as these, may be explained when the general relation of radium rays to fundamental biologic phenomena are better known.

References

Bryant, W. S. Radium in middle ear deafness caused by chronic suppuration. *N. York M. J.*, 100: 7, 1914.

Sobotky, I. Radium treatment of tinnitus and middle ear deafness. *N. York M. J.*, 105: 1138, 1917.

Stevenson, W. C., and Wilson, T. C. Rationale of radium treatment of middle ear deafness, with preliminary report of its effect on chronic hyperplastic otitis media. *Irish J. M. Sc.*, pp. 630–634, Nov., 1926.

Polyps (nasal)

Diagnosis is not discussed in this outline but should be established by every possible means. (See p. 13.)

Pathology. The common form of nasal or myxedematous nasal polyp referred to in this group is probably a chronic reaction on the part of the nasal mucous membrane to a

chronic inflammatory process in the accessory nasal sinuses. The masses are multiple, soft, translucent, edematous, pedunculated, arising about or within the communicating openings between the accessory nasal sinuses and the nasal cavity. Obstruction to breathing and hindrance to free drainage from the sinuses are the chief secondary results from multiple nasal polyps of size. The structure of polypi consists chiefly of an intercellular edema of varying degrees between fibrous strands and slightly or greatly increased mucous membrane epithelium. Progressive enlargement, increase in number, and elongation of pedicle comprise the course of nasal polyp development. Malignant degeneration is rare. Chronic inflammation of the sinus probably causes polypoid inflammation and in turn polypoid inflammation is certainly aggravated by sinus infection.

Radium Indications. The structure of nasal polyps is such that radium rays have little but a drying and atrophying indirect effect upon them due to endarteritis and increase in fibrous tissue formation following the initial shrinkage. Ordinarily polypi are removed surgically, but they commonly recur time after time. Radium applied to the site after surgical removal inhibits the activity of the mucous membrane directly, decreases vascularity by endarteritis and increases fibrosis and shrinking of the nasal mucous membrane with the ultimate appearance of atrophy; so the process may not be strictly a glandular atrophy.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The cavity application of screened radium or radon in tubes to the site of excised nasal polyps is the method commonly employed in their treatment with radium. From 50 to 100 mg.-hr. screened to allow 5 to 10 per cent of the beta rays to penetrate the mucous membrane, packed firmly against the probable site of recurrence, suffices to inhibit the recurrence of polyps. A second, and not uncommonly a third application, each following surgical excision by a few days, are sometimes required.

Reaction. A general reaction is absent. Locally, there is rarely a marked inflammatory reaction following dosage

up to 100 mg.-hr. Slight redness and swelling may be seen, with occasionally a white exudate. Persistence of the etiologic chronic inflammatory process may cause recurrence in spite of radium treatment. The recurrences appear after a longer delay because of the radium treatment, and when they do appear they are apt to be more fibrous than formerly. Second excision and postoperative irradiation are followed by delayed and reduced recurrence or none at all. The third application practically always clears up the condition. Favorable cases do not recur after the second application and practically all disappear after the third treatment. Unfavorable cases recur repeatedly. It is probable that the site of recurrence is located within the sinuses, just beyond the inhibiting influence of the rays, on account of the increased distance from the radium.

Prognosis. Two or three postoperative radium applications to nasal polypi can be depended upon to prevent recurrence in the large majority of cases.

Case History

Mr. C. Aged forty. Nasal polyps. Polyps in nose present for several years. Operated one year previous. Recurrence greater than original. Surgical removal followed by radium. Treated by 50 mg. in each side for two hours, beta ray screen, 200 mg.-hr. No recurrence. Rapid relief from sinusitis. Well one year.

References

Lyons, H. R. The use of radium in the treatment of myxomatous nasal polyps. *Am. J. Roentgenol.*, 8: 407, 1921.

Lyons, H. R. Treatment by radium of nasal polyps. *Am. J. Roentgenol.*, 9: 584, 1922.

Epithelioma of the Ear, Eyelid and Nose

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. Squamous-celled carcinoma of the ear, eyelid or nose does not differ from epidermoid carcinoma elsewhere, except that it easily invades cartilage. Epithelioma in either of these locations is ordinarily slow growing, with successive stages of ulceration, crusting and healing, spreading peripherally, and eventually invading nasal, tarsal, or aural cartilages. Metastasis is rare. Extension is

gradual but eventually the cartilage is completely eroded. If the eyelid is involved, the conjunctiva and intraorbital structures are later destroyed. Secondary growths finally appear in the draining lymph nodes after the cartilage has become involved. There follows, when untreated, complete destruction of the contents of the orbit in the eye cases, of the nasal cartilages and bones in the nose cases, and of the external ear and eventually the bony structures of the auditory canal in ear cases.

Radium Indications. Radium is undoubtedly indicated in epithelioma of these locations. It is well adapted for complete destruction of the early lesions. After cartilage has been invaded, radium is able apparently to destroy the malignant cells, but healing is protracted or may not occur at all. Erosion proceeds to complete destruction in spite of all efforts. Cartilage has little power to recover from the caustic action of radium rays. Either the malignant cells in cartilage cannot be completely destroyed or the protective power and healing properties of the tissues are not sufficient on account of poor blood supply. At any rate, cartilage once involved by epidermoid carcinoma rarely heals.

Inhibition of the growth and probably greatly delayed progress follow careful irradiation with gamma rays. Clinical cure by radium alone is doubtful in advanced cartilaginous involvement.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. For the early superficial growths, radium element in flat applicators of full strength is indicated. Lead plates are placed over the lesion protecting the surrounding healthy skin, with apertures the shape of the lesion but larger in all diameters by 2 to 4 mm. Plaques covered only with rubber for cleanliness may be placed over the aperture. Exposures of full strength plaques for from one to four or five hours should suffice for complete destruction of malignant tissue. When the lesion is more than 2 to 3 mm. thick, the soft rays are best reinforced with gamma rays to the extent of 60 to 70 mg.-hr. per square centimeter, placing the

additional radium on top of the plaque, thus insuring gamma ray penetration only. Tubes or needles with a screen of from 0.4 mm. of steel to 0.5 mm. of silver may be used in lieu of plaques, raising the radium away from the lesion 2 or 3 mm. to produce a more nearly homogeneous irradiation of the lesion with a dosage of 60 to 75 mg.-hr. per square centimeter.

Extensive lesions are perhaps best treated by deep external irradiation, thus avoiding, if possible, the caustic action of the soft rays. Early lesions are ordinarily cleared up with one application. However, when cartilage is involved, repeated irradiations are made at intervals of one to three months when recurrences or extensions become evident.

Reaction. The general reaction is scarcely noticeable in early superficial lesions. When heavy beta and gamma irradiation is given over a large area, malaise, headache and general discomfort may result secondary to the local reaction.

Locally the inflammatory reaction begins from five to ten days after treatment. Redness, swelling, pain and disintegration, with moisture and sloughing or crust formation follow in sequence during the next two to three weeks. By the fifth week repair is in progress and healing begins. When cartilage is extensively eroded the evidences of a repair process are scant Contraction, fibrous tissue formation and epithelial new growth from the periphery are extremely slow to appear, if at all. By the sixth or seventh week, regrowth or continued erosion is evident and re-treatment is all that can be offered by radium. In the end the whole ear, nose or tarsal cartilage are completely destroyed with subsequent invasion of bone or orbit and uncontrollable spread of the disease. Some surgical or mechanical removal of the ulcerated tissue by wide destruction is indicated.

Prognosis. Early lesions heal permanently. When cartilage is extensively involved, progress may be delayed; but slowly the whole organ yields to invasion and the ultimate prognosis is extremely grave.

Case History

Miss N. Aged fifty-five. Epithelioma of nose. Ulcerated, raised, slightly crusted lesion 1.5 cm. in diameter at the junetion of cheek and right ala nasae. Present one year. Raised pearly edges. Treated by 10 mg. radium in full

strength plaque for two hours, protecting surrounding normal tissue with lead foil 1mm. thick. No screen to radium. Clinically well two years.

References

Greenwood. Epithelioma of the nose, showing the result of radium treatment. *Arch. Dermat. & Syph.*, 7: 857, 1923.

Mathey-Cornat, R. and Barrat, P. Roentgen and radium therapy in cutaneous epitheliomata of the nose. *Rev. de laryngol., etc.*, 45: 733; 779, 1924.

Pfahler, G. E. Electrocoagulation and radiation therapy in malignant disease of the ear, nose and throat. *J. A. M. A.*, 85: 344, 1925.

Queyrat, L., and Degrais. Epithelioma of the nose, eye and cheek, of eight years' duration. *Bull. Soc. franc. de dermat. et de syph.*, 28: 363, 1921.

Simpson, C. A. Radium treatment of malignancy of the eyelid. *Urol. & Cutan. Rev.*, 28: 276, 1924.

Keloids

Diagnosis is not discussed in this outline but should be established as thoroughly as possible in every possible instance. (See p. 13.)

Pathology. Keloids are composed of bands and bundles of wide, fibrous strands with little elastic tissue. There is a congenital predisposition to excessive connective tissue formation. These lesions follow wounds, burns, common lacerations, and extend far beyond the normal scar tissue formation. The colored race is especially susceptible. The lesions are deforming, progressive, occasionally regressive, and occasionally painful. The thickened fibrous bands stiffen the skin and may grow to an enormous size.

Radium Indications. The beta and gamma rays of radium cause the absorption of these tissues and their replacement by a scant, fine fibrous tissue. There is also relief from pain in most cases. The lesions are easy of access for observation and treatment. In extensive lesions repeated treatments with gamma radiation may be necessary over a considerable period of time. Radium therapy decreases the likelihood of malignant degeneration; it is also valuable as a prophylactic, following the excision of keloids and after operation in keloidal patients, to deter the formation of a keloid in the surgical incision.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The smaller lesions may be eradicated by means of the beta rays, lightly screened, perhaps 0.1 mm. of lead and rubber, thus making use of the caustic action of the rays. A windowed lead sheet protects the normal surrounding skin in the one or two treatments ordinarily required. Extensive lesions or those 2.0 mm. or more in thickness require the gamma ray, with a suberythema dose. Applications of from 200 to 1200 mg.-hr. per 2 sq. in. of surface at 1 inch distance, repeated at intervals of two, three or four months, cause the gradual disappearance of these extensive lesions. When the distance is less than 1 inch, the milligram-hour dosage may be decreased below 1200, the total dosage decreasing according to the inverse square law governing all radiant energy. Treatments may extend over months or even years.

Reaction. When the caustic dose is employed, the inflammatory reaction proceeds from the initial redness to the production of moisture and the formation of a crust, which thickens, dries and finally separates six to eight weeks later. A fine tissue-paper scar remains at the site of the keloid. A mild brownish pigmentation may appear subsequently, and occasionally telangiectasis in the scar and at the periphery. The treatments with gamma rays gradually cause the absorption of the thick, fibrous bands, resulting in increased pliability and decreased thickness of the lesion, although the completion of these processes may require months or years. The limitation of motion due to the thickness of the lesion is relieved, and function improved as pliability increases. There is no scarring with this method of treatment. Malignant degeneration in a keloid is extremely refractory to radium.

Prognosis. The prognosis is good. Complete destruction of small lesions is easily accomplished. Recurrence is the exception. In extensive deforming lesions the maximum of reduction may be accomplished, function restored, pain relieved, and malignant degeneration forestalled. Fear has been expressed regarding the advisability of treating keloids forming on the site of a burn. In our opinion malignant degeneration is probably less apt to occur in keloids treated

with radium than in untreated keloids of this nature. The end results in all efficiently treated keloids are gratifying.

Case History

Mr. W. Aged twenty-six. Keloid. Raised, smooth, pink, tender scar 1.5 cm. diameter, on back of neck at site of healed furuncle. Increasing in size and sensitiveness. Treated by a 10 mg. full-strength plaque of radium over lesion for four hours, screened with 0.1 mm. of lead and 0.7 mm. of rubber. Flat, white, pliable, painless scar in three months.

References

Daland, E. M. Radium treatment of keloid. *Surg., Gynec. & Obst.*, 36: 63, 1923.

Hazen, H. H. The roentgen ray treatment of keloids. *Am. J. Roentgenol.*, 11: 547, 1924.

Kurtz, H. B. Radium in keloid and cauliflower growths on same following extensive burns. *Urol. & Cutan. Rev.*, 24: 196, 1920.

Sainz, de A. Surgical measures combined with radium in the treatment of elevated keloid. *Siglo. med.*, 72: 1185, 1923.

Simpson, F. E. Radium in the treatment of keloids. *J. A. M. A.*, 64: 1300, 1915.

Stevenson, W. C. Radium treatment of scars. *Lancet*, 1: 432, 1918.

Stevenson, W. C. The technic of the after-treatment of war injuries. by radium. *Arch. Radiol. & Electroth.* 23: 356, 1918–19.

Taft, A. R. The treatment of keloid by radium. *Urol. & Cutan. Rev.*, 22: 31, 1918.

Taft, A. R. A review of keloid cases treated with radiotherapy. *Urol. & Cutan. Rev.*, 27: 755, 1923.

Taussig, L. R. The treatment of keloids with radium. *California State J. M.*, 21: 520, 1923.

Keratoses (senile and roentgen-ray)

Diagnosis is not discussed in this outline but should be established as thoroughly as possible in every instance. (See p. 13.)

Pathology. These lesions are formed by thickening of the epithelium in localized elevated areas. They are often crusted, resembling epitheliomata, except for the indurated, raised edges. They may be multiple. The common sites for senile keratosis are the face and hands. They are seen in late adult life on skin exposed to weather and other irritative agents. In the case of roentgen-ray keratoses the roentgen ray is, of course, the irritative agent. A dermatitis usually precedes the keratosis, which begins as a scaling on top of the thickened base which scaling later becomes a crust.

Some of these crusted areas may ulcerate. Often they become painful and they occasionally undergo malignant degeneration with erosion and tissue destruction.

Radium Indications. Radium rays are suitable for the destruction and cure of senile keratoses. The lesions are accessible for treatment and observation. Keratoses due to the roentgen rays yield very readily to brief applications of beta rays of radium to the surface of the lesion.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Unscreened, full-strength glazed plaques, over windowed lead, may be applied from one to four hours in cases of senile keratoses. The duration of the application depends largely upon the thickness of the crust, the more superficial requiring the shorter applications. When the crust is thicker than 2.0 or 3.0 mm. the gamma rays from 25 to 50 mg. of radium should be used to reenforce the beta rays from the plaque. The removal of crusts before the radium crust is thicker than 2.0 or 3.0 mm. the rays from 25 to 50 mg. of radium should be used to reenforce the beta rays from the plaque. The removal of crusts before the radium treatment is often unjustifiable on account of the production of an ulceration. Roentgen keratoses require but a few minutes of treatment, as they seem to be exceptionally susceptible to the beta rays. One exposure with a full-strength plaque, lasting from three to five, rarely ten, minutes, clears up lesions on the hand, which is the usual location. Repetition is seldom required for the same area. Other areas may develop and many treatments are often given to the same patient. The use of screened radium in these lesions should be avoided.

Reaction. There is no general reaction from these applications. In the case of senile keratoses, the local inflammation begins within ten days as a redness about the periphery and an increase in the thickness of the crust, reaching a height of 4.0 to 8.0 mm. in some cases. Drying and separation of the crust are accomplished in about six weeks in the average case. In roentgen lesions there is little reaction except a drying and a separation of the scales and in three or four

weeks a subsidence of the red, inflamed condition. The end results in senile lesions are characterized by smooth, white, tissue-paper scars, scarcely noticeable; occasionally they will recur in from two to six months, usually in instances where insufficient gamma or hard beta ray applications were employed.

PROGNOSIS. Excellent results are obtained in senile keratoses. Practically all lesions are cleared up permanently. Roentgen-ray keratoses yield month after month, until rapid invasion or neglect allows one of them to degenerate; then heavy irradiation is accompanied by a good deal of risk, and there is danger of extensive breaking down with the formation of intractable ulcers exhibiting a proneness to degenerate into malignancy.

CASE HISTORY

Mrs. S. Aged fifty. Keratosis. Crusted area 1.0 by 0.7 cm. No induration or raised edge. No excavation. Present many months without itching. Treated by 10 mg. full-strength plaque of radium screened with 0.7 mm. rubber, over crusted area for two and one-quarter hours, using lead foil 1 mm. thick to protect surrounding normal skin. Pale flat scar seen two years later.

REFERENCES

BURNS, F. S., and BLAISDELL, J. H. The use of radium in the treatment of cutaneous epithelioma and keratosis senilis. *Boston M. & S. J.*, 176: 774, 1917.

DEGRAIS P., and BELLOT. Radium in x-ray burns. *Presse méd.*, Jan. 28: 364, 1920.

FABRY, J. Treatment of a severe roentgen burn of the hands with radium and doramad salve. *Med. Klinik.*, 21: 1498, 1925.

TOUSEY, S. Roentgen-ray keratoses on hand of roentgenologist cured by radium. *J. A. M. A.*, 64: 1394, 1915.

LEUCOPLAKIA

Diagnosis is not discussed in this outline but should be established by every possible means. (See p. 13.)

PATHOLOGY. These lesions are keratinized thickenings of the mucous membrane ordinarily of the mouth, occasionally of the vulva and vagina. They are flat, pearly patches, becoming thicker, more elevated, and later densely adherent, fissured, and prone to epithelial degeneration. They are found at sites of chronic irritation, often associated with

jagged teeth, ill-fitting plates, syphilis, and the use of tobacco. Patients are susceptible to recurrences if the etiologic factors are not eradicated.

Radium Indications. The soft beta rays of radium are capable of clearing these lesions in small doses without loss of tissue. They are usually easy of access for treatment and observation.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Surface homogeneous treatments usually accomplish a cure, in superficial types of lesions, using glazed full-strength plaques over the surface for fifteen to forty-five minutes, screened only with rubber. Bare glass tubes may be used in lieu of plaques by giving 2 to 4 mg.-hr. per square centimeter of area, but the tube must be kept in constant motion to accomplish homogeneous irradiation. Screened radium is less certain in superficial lesions. Densely adherent, thickened lesions with fissures require longer applications or radium so screened as to permit the use of 10 to 20 per cent of the hard beta rays. Exposure should be from 5 to 10 mg.-hr. per square centimeter of tissue. One treatment usually suffices. In deeper lesions, where there is the slightest suspicion of epithelial degeneration, the interstitial method of application with element needles or gold implants is required, the needles being placed parallel, 1 cm. apart, 2 to 3 mm. below the base of the lesion, in dosage of 40 to 75 mg.-hr. per cubic centimeter of tissue. Irradiation should extend 1 cm. beyond the clinical border of the lesion. One treatment usually suffices. Re-treatment may be given in four weeks to missed areas. Adjacent, scattered lesions not infrequently appear in susceptible patients and re-treatment is indicated.

Reaction. There is no general reaction. Locally, the inflammatory reaction, which begins within five days, is characterized by redness, swelling, and ulceration, superficial in type, with the sloughing-off of the keratinized tissues. The ulceration usually heals by the fourth week. Recurrence *in situ* is uncommon after efficient irradiation. The interstitial treatment results in a more marked reac-

tion. Inflammatory swelling is greater, beginning in from five to ten days, progressing slowly, with ulceration and sloughing in the third week, and healing often delayed to the fifth or sixth week. The swelling and inflammatory reaction are usually much more marked in vulvar lesions. Re-treatments in the seventh or eighth week may be indicated for management of missed areas or to compensate for inefficient initial treatment. Smaller dosage in later treatments is advised on account of fibrosis and danger of extensive slough with intractable ulcers. Recurrence in adjacent areas is not uncommon. The end result in favorable cases is a smooth, unscarred, normal mucous membrane with no depression, except in lesions extensive at the outset.

Prognosis. Practically all leucoplakias yield permanently to efficient radium treatment. Failures are usually due to inefficient irradiation of the depth of the lesions. It is preferable to use the interstitial treatment, even though more severe, than to run the risk of recurrence. Since leucoplakia is acknowledged to be a precancerous lesion, the efficient treatment of this condition is one of our great hopes for the control of cancer.

Case History

Mr. B. Aged seventy-three. Leucoplakia. Entire mucous membrane of lower lip covered with a white adherent membrane. Small area of ulceration in center of lesion. Surgical removal of epithelioma of lip six years previous. Patient had radium and is sensitive to it. Full-strength plaques for twelve minutes over entire lesion, screened with 0.7 mm. of rubber. Severe reaction with ulceration out of proportion to treatment. Healed in one month. Well three years.

References

Boggs, R. H. The treatment of leukoplakia by radium. *Texas M. J.*, 32: 224, 1916.

Pinch, A. E. H. Chronic superficial glossitis; leukoplakia of the tongue. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 49, 1923.

Lichen Planus

Diagnosis is not discussed in this outline but should be thoroughly established in every instance. (See p. 13.)

Pathology. These lesions are chronic, inflammatory processes, often saccular, frequently scaling, rarely crusting, about the hair follicles of the skin, or at the site of pustules. The disease is not self-limited. Itching is often intolerable. The sites are multiple, the lesions increase often in size.

Radium Indications. The soft beta rays of radium relieve the itching and cause involution. This effect is probably due to the property of radium radiation to stimulate and to produce local leucocytosis. The lesions are easy of access for treatment and observation. If they are very extensive, the treatment is tedious but it can be accomplished.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Full-strength, glazed flat applicators are best suited to obtain homogeneous irradiation. The duration of the treatment should be kept well under the erythema dose for the normal skin, beginning with an exposure of one minute per area with radium screened only with rubber. A progressively increased dose should be applied at intervals of four or five days until the therapeutic dose is reached. Relief of pruritus is early accomplished with dosages under five minutes per area. The lesions should be carefully mapped out to prevent overlapping, or the therapist should keep the applicator in continuous movement over the skin involved for one to five minutes per area in order to accomplish homogeneous irradiation. The dosage may be repeated in ten days if no reaction is accomplished. The therapeutic dose should be ascertained as quickly as possible. Thereafter, the treatment may be repeated at three week intervals, giving full time for the recovery of each area from the reaction. The ulcerating dose should be avoided with its consequent scar formation and subsequent contraction. Lesions which have become thickened because of the chronicity of the disease require longer applications with the radium screened with some metal, for example, 0.1 mm. of lead, in order that the depth may be reached without undue destruction of the upper layers of the skin.

Reaction. The therapeutic dose yields relief from itching and hyperesthesia within a few days. Ten days sees an

increase in the inflammation from slight to marked, with scaling, drying, increased pallor, decrease in thickness, and general subsidence of the lesion. If the depth is reached by means of longer applications and a metal screen, thicker lesions yield more slowly. However, if the depth of the lesion is not reached, recurrences are frequent. The end results present a smooth, healed, non-inflammatory skin which may show slight atrophy or slight scarring from the disease rather than from the radium reaction.

PROGNOSIS. Pruritus is easily and often completely relieved. A fair percentage of the cases are clinically cured. Deep-seated lesions are apt to recur. Radium is a valuable and reliable aid in the treatment of chronic, persistent lesions.

LUPUS VULGARIS AND ERYTHEMATOSUS

Diagnosis is not discussed in this outline but should be established by biopsy when desirable. (See p. 13.)

PATHOLOGY. Lupus vulgaris is an infectious granuloma of the true tuberculous type. It contains nodules which are miliary in character and often contain the tubercle bacilli. These lesions usually attack the face, giving rise to ulceration, local leucocytosis, increase in fibrous tissue, and resulting in deforming scars. Recurrences are common. Lupus erythematosus is not a true tuberculous process, but is characterized by small inflamed areas of the skin with crusting or scaling. Isolated patches are common on the face, but the classical butterfly lesion over the bridge of the nose is not so commonly seen as formerly. This lesion is a chronic inflammatory process of the skin, more superficial than vulgaris.

RADIUM INDICATIONS. Small doses of the beta rays of radium suffice to clear up many of the cases. These lesions are readily accessible for treatment and observation. The alterative action of the rays seems to be responsible for the therapeutic effect in these conditions. The treatment is simple and scarring is kept to a minimum. Light or roentgen-ray therapy is more commonly used in lupus.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Full-strength glazed plaques, covered with rubber, may be applied to the surface from ten to thirty minutes, depending upon the thickness of the lesion. Shorter applications are better made at the outset, at two or three week intervals to determine the tolerance of the lesion to the radium. The treatment should extend 2.0 or 3.0 mm. beyond the clinical margin. A mild inflammatory reaction should be sought but no ulceration is desirable or necessary. The lesions of lupus erythematosus especially require shorter applications and more careful irradiation to avoid a marked inflammatory reaction. In the case of lupus vulgaris, when the lesions are thicker than 2 mm., gamma rays should be employed to reach the depth. One hundred to 300 mg.-hr. at ½ inch over each 2 sq. in. is a fair standard of dosage in gamma ray application to these lesions. Failures and recurrences are probably most often due to failure to reach the depth of the lesion. Individual lesions in individual cases require special adaptation of increasing dosage. The reaction should be mild to moderate. Treatments may be repeated in three weeks according to the reaction and the results obtained up to the moment.

Reaction. There is no general reaction. In lupus vulgaris, the local reaction is mild, characterized by an inflammatory redness with moisture, especially in ulcerated lesions. In dry lesions scaling and crusting may be temporarily increased. The reaction subsides in three to four weeks. Re-treatment is indicated according to insufficient treatment, missed areas, depth recurrence or extension of the lesion. Recurrences may appear at neighboring sites as early as three months, or at the site of the old scar. In the erythematosus form the reaction is usually a mild erythema with scaling which subsides within three weeks. Treatments may be repeated in three to four weeks, according to the result obtained in the earlier treatment.

Prognosis. The prognosis in these lesions is usually good, although not invariably so. The most common failure is traceable to insufficient depth reaction. Success depends upon a careful study of the lesion and a gradually increasing dose adjusted to the reaction within the lesion, avoiding a dosage sufficient to affect the normal skin. Failures are

often due to irregular observation and treatment and inefficient technic.

References

Aikins, W. H. B. Radium in tuberculosis of the skin. *Canad. Pract. & Rev.*, 43: 42, 1918.

Kumer, L., and Sallmann, L. Radium therapy of tuberculous diseases of the eyelids, etc. *Ztschr. f. Augenhlk.*, 54: 11, 1924.

Mackay, H. Lupus erythematosus and its treatment by radium. *Canad. M. A. J.*, 15: 14, 1925.

Pinch, A. E. H. Lupus vulgaris of the palate. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 52, 1923.

Du Casse, P. R. Sycosis vulgaris and radium. *Ohio State M. J.*, 20: 357, 1924.

Foerster, O. H. Radium in dermatology. *Arch. Dermat. & Syph.*, 9: 38, 1924.

Lymphangioma (lymphangiectasis, macrochilia and macroglossia)

Diagnosis is not discussed in this outline but should be established by biopsy whenever this seems necessary (See p. 13.)

Pathology. These lesions are congenital dilatations of lymphatics, slowing up the lymph flow; if occurring in the lymphatics of the lip, the condition is known as macrochilia, if in the tongue, macroglossia. The lesions are associated with varying degrees of hemangioma or endothelioma, and are rarely found alone. They are types of elephantiasis. Enlargement and engorgement of the lip or tongue results in deformity, marked thickening and susceptibility to trauma and local infection. Pliability of the parts is reduced, and the disfigurement is often marked.

Radium Indications. Hard beta and gamma rays from radium are capable of reducing these lesions by obliteration of the channels by causing swelling and proliferation of the endothelial cells. They are easy of access for treatment and observation. No scarring, discomfort, or loss of structure follows the treatment. Acute infection contraindicates local treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Heavily screened radium or radon is most efficient when applied by means of the deep external irradiation method at various distances, with dosage from 50 to 100 mg.-hr. per square centimeter of surface area, at 1 inch distance. Irradiation within the mouth or inside the lip reduced as the square of the distance to avoid local inflammatory reaction should be employed. All possible cross-fire should be made use of, avoiding any local skin or mucous membrane reaction. Treatments may be given at intervals of six to eight weeks over several months and over as long a period as two years. They should be continued until the lesion has almost disappeared or until the condition remains stationary for three or four months, indicating that further shrinkage will probably not be obtained. Interstitial treatment using element needles or radon implants may be used in dosage of 30 to 60 mg.-hr. or mc.-hr. per cubic centimeter.

Reaction. There is no general reaction except when large doses amounting to 3 to 5 gm.-hr. are given at one sitting, in which case there will be malaise. Locally, there should be no visible reaction except an occasional, slight swelling when heavy dosage is applied, evident between the fifth and the fifteenth day. This swelling is transient. After several months shrinkage gradually occurs, continuing for an indefinite period thereafter. The end results approach the normal size and consistency of the part, except where increased fibrosis of the original lesion prevents any further shrinkage. There is no change in the skin or mucous membrane following efficient treatment, except possible dryness of the skin or mucous membrane and increased viscosity of the salivary secretions. Slight dryness of the mouth and sometimes mild hyperesthesias may be present for many months. Occasionally erysipelas may complicate the reaction. An inadvertent inflammatory local reaction sometimes occurs. Recurrences do not take place.

Prognosis. Practically all lymphangiomatous lesions improve gradually by reduction in size. The deformity is reduced, function is improved, and cosmetic results are usually satisfactory. No untoward results occur when conservative technic has been followed, avoiding reactions in skin and mucous membrane. Patience must be exercised

and there must be restraint on the part of the radiologist and the patient during the process.

Case History

Miss H. Aged twenty-one. Lymphangioma. Mucous membrane of right cheek and right upper lip roughened, streaked with a few dilated vessels and islands or tufts of capillaries; the entire cheek and upper lip are thickened to twice the normal, causing a very noticeable deformity, easily seen at a distance of many feet. Both surfaces of tongue involved in the same manner. Tissues itch, pain and occasionally bleed, and are swollen when there is a "cold." Present since birth. Treatments externally, with from 50 to 100 mg. of radium at 1 inch distance, using the beta ray screen, averaging 600 mg.-hr. per treatment. Intervals, six weeks. One hundred to 300 mg.-hr., with beta ray screen, at 0.5 cm. distance, over inside of cheek and dorsal and ventral surface of the tongue, at four month intervals. Total irradiation over one year 6000 mg.-hr. Disappearance of roughness and surface blood vessels. No pain. Deformity reduced until it could not be recognized at more than 3 feet. Erysipelas accompanying a "cold" developed after one treatment. Five years' observation.

References

New, G. B. Radium in the treatment of lymphangioma of the tongue. *Journal-Lancet*, 36: 699, 1916.

Pinch, A. E. H. Angioma and lymphangioma of the tongue. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 49, 1923.

Simpson, F. E. Radium in the treatment of lymphangioma circumscriptum. *J. A. M. A.*, 66: 949, 1916.

Melanoma (melanoepithelioma and melanosarcoma)

Diagnosis is not discussed in this outline but should be established by biopsy in every posssible instance. (See p. 13.)

Pathology. This group includes melanin-bearing tumors of any type. Growths which have been quiescent may become active at any time. Melanoepithelioma is the more common of the two. Rapid growth with evident clinical change indicates the sudden transition to malignancy of otherwise benign moles. Very soon numerous and extensive secondary growths appear. The malignancy is of the very highest degree. Subsurface tumors containing melanin and exhibiting characteristics of rapid growth are ordinarily of the melanosarcoma type. A diagnosis of these masses is seldom made except after excision.

Radium Indications. Radium is the best agent for the destruction of these highly malignant tumors. The caustic action should be employed to accomplish the complete local destruction of the masses. The beta rays are best fitted for this purpose; radium therapy excels all other forms of treatment in that its action is accompanied by a minimum of mechanical disturbance and a maximum destructive power insidious in its method.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Preliminary deep external irradiation to seal lymphatics as far as possible is the first step in the treatment. Intense irradiation with an applicator containing from 1 to 4 gm. of radium at 6, 10, or 15 cm. distance probably gives the best promise of success. Interstitial application of radium element in needles or of radon implants is then justifiable in treating subsurface tumors. Complete cautery destruction is sought. Normal structures must be sacrificed to insure 100 per cent eradication of the growth. Dosage of 100 to 130 mg.-hr. per cubic centimeter of tissue is justifiable when needles are employed. Glass implants containing from 1.0 to 1.5 mc. or gold implants containing 2 to 3 mc. each are advisable in each cubic centimeter of tissue. Many of these tumors are amenable to treatment while confined to the skin surface, where they may be treated with full-strength glazed plaques. The time of application varies from six to twelve hours per area involved. Complete destruction down to the fascia is indicated. The imbedding of needles or implants in the depth of the wounds after operative removal or after biopsy is advisable. Second applications are of doubtful value.

Reaction. The general reaction is not marked unless a dose of 5 to 10 gm.-hr. is administered. Locally the inflammatory swelling, ulceration and crust formation, with continued thickening of the crust, continues for about six weeks. Separation of the crust occurs ordinarily from the sixth to the eighth week. A smooth, white, depressed scar appears at the site of the tumor in successful cases. If secondary growths are present radium treatment is of

questionable value. Subsurface lesions may slough *en masse;* healing is then protracted. Plastic surgery may repair the defect if the cases remain clinically well. Dissemination is rapid and death occurs within seven or eight weeks in unsuccessful cases.

Prognosis. In subsurface tumors, which are seldom recognized except under the microscope, the prognosis is grave, almost hopeless. If secondary growths are present at the time of diagnosis, treatment is of little value. Suspicious surface lesions should be removed by means of radium. Rapid local changes in a pigmented mole indicate possible malignancy; this may often be cured permanently with radium alone.

Case History

H. C. Aged fifty-one. Melanoma. Black mole on dorsum of foot since birth, Struck by corner of box four months ago. Lesion began to enlarge and thicken. Now presents a raised lesion, measuring 1.5 cm. at base, raised 0.5 cm. involving one-eighth of original lesion. Top ulcerated. No palpable glands. Treated by 2400 mg.-hr., with 100 mg. radium, at 1 inch distance, over two areas. Five days later 10 mg. full-strength plaque, unscreened, against lesion for ten hours. Total dosage 2500 mg.-hr. Lesion mummified and dried up in three months. Quiescent sixteen months.

References

De Santi, P. R. W. Melanotic sarcoma of the septum nasi. *Brit. M. J.*, 109, 1925.

Heckel, E. B. Report of a case of melanosarcoma of the orbit treated with radium. *Arch. Ophth.*, 45: 465, 1916.

Wilder, W. H. Melanotic epibulbar tumor dispelled by the use of radium. *Arch. Ophth.*, 53: 355, 1924.

Mycosis Fungoides

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

This rare lesion is diagnosed with difficulty and often not decisively. Microscopically it cannot be distinguished from carcinoma in many instances. By many it is interpreted as a chronic inflammatory lesion. Caustic destruction of the bulk of the hypertrophic ulcerating mass can be accomplished with radium. Healing is protracted. Complete clinical cure has not been seen in lesions several inches in diameter. Smaller superficial lesions can be made to heal with doses of

20 to 50 mg.-hr. per square centimeter of surface, employing a screen transmitting 10 to 15 per cent of the beta rays. Secondary acute pyogenic infection may delay the application. The reaction is generally not severe, though the local slough may be extensive. Complete clinical cure of isolated single lesions can be accomplished but in instances of raised ulcerated lesions several inches in diameter the destruction of adjacent normal tissues or their devitalization is so marked that it is almost impossible to secure permanent healing.

Case History

Mr. S. Aged forty-one. Mycosis fungoides. History of scaling, itching, erythematous skin lesions more or less general over the body for twenty years. Four years ago several of the lesions of the skin began to manifest hypertrophy and later to ulcerate in various sites, the chief being on the chest and left arm. The arm lesion measured 3.0 by 4.0 cm. and was raised 0.5 cm. The lesion on the left chest measured 15 cm. in diameter and was raised 2.0 cm., with an ulcerating, fungating surface. Patient received 27,000 mg.-hr. of radium, with the beta ray screen, over skin surface about the periphery of the lesions, allowing 12 per cent beta rays to penetrate when ulcerated areas were treated. Seventeen treatments extended over six months of time. All lesions except that on chest healed. This large lesion would not yield. Patient died of the disease six months after last radium application apparently from sudden collapse of the lung. (Microscopic diagnosis on two occasions late in the course of the disease: squamous-celled carcinoma.)

Nevus (pigmented)

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. A pigmented mole or nevus is a circumscribed lesion of the skin, characterized by an accumulation of melanin within the epithelial cells of the corium. Within the pigmented area, changes in the hair, hyperkeratosis or warty formation and areas of hemangiomatous nature frequently are found and there is a tendency to spread or degenerate into a malignant melanin-bearing epithelioma. The lesions are usually present from birth; they may be multiple, and they may be very extensive. The majority are borne through life without clinical manifestations, but occasionally an intensely malignant melanoepithelioma develops from one of these pigmented nevi.

Radium Indications. The caustic action of the beta rays of radium is well fitted to completely destroy the melanin-bearing cells of the skin. If destruction of the lesion is desirable on account of changes in size, shape, symptoms or character, radium offers the safest method with a minimum of trauma and an ideally insidious attack upon these degenerating areas.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. These lesions occurring on the exposed portions of the body may readily be destroyed by full-strength glazed plaques applied for a period of two to five hours per area. Lesions thicker than 3 mm. require heavier treatment, often reenforced by gamma rays. Complete epilation is accomplished with this dosage. If the lesion is small, lead foil shields may be used to protect the surrounding normal skin while the therapeutic rays are passed through an opening of the shape of the lesion but having a diameter 1 or 2 mm. greater. Rarely are second applications necessary.

Reaction. There is no general reaction. Locally the inflammatory changes begin within a few days, and are characterized by redness, swelling, exudation of serum from necrosis of the surface cells with crust formation, and a gradual thickening of this crust from the accumulation of debris as the deeper lying cells are destroyed and additional serum added. By the end of the third week the destructive process is practically completed and the separation of the crust begins to be in evidence. Complete separation is accomplished in from four to six weeks, depending upon the depth of the reaction. In favorable cases a pale, white, slightly depressed scar results, occasionally with small dots of pigment remaining, indicating the depressions of the melanin-bearing epithelium into the skin. One hundred per cent removal of the pigment cannot be accomplished unless necrosis is produced as deep as the subcutaneous fascia. The lesions do not recur.

Prognosis. Innocent, disfiguring pigmented nevi can readily be removed from the skin; frequently they are removed for cosmetic reasons.

Case History

Mr. D. Aged fifty. Nevus pigmentosa. Dark, slightly raised area 1.0 by 0.6 cm. located on left abdominal wall. Present for many years, increasing in size, slightly reddened. Treated by 10 mg. full-strength radium plaque over windowed lead for two hours, unscreened. Lesion disappeared leaving low white scar without pigmentation. Eighteen months.

Paget's Disease of the Nipple

Diagnosis is not discussed in this outline, but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. This lesion is characterized by an eczematous inflammation of the nipple. Redness, slight swelling, crusting, or scaling, with occasional weeping and crust formation, gradually extending to include the whole areola, are the common early findings in Paget's disease. The condition is chronic and in its later stages is characterized by induration of the skin, retraction of the nipple, and fissure or ulcer formation; very often there is an eventual malignant degeneration. The condition may last for months or years without serious outcome. When malignant degeneration does occur, the cells are of the squamous type and tend to spread peripherally and dip down into the parenchyma of the mammary gland. Ulceration, induration, pain, and bleeding occur late and metastases are uncommon.

Radium Indications. Early lesions are easily eradicated by small doses of soft rays, such as is given in simple eczema. It is probably the alterative or local leucocytic property of the radium rays which brings about the results in this condition. Deeper seated, more chronic lesions require the screened rays to reach the depth of the pathology.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Early lesions are adequately treated by means of surface application of lightly screened or unscreened radium, probably best applied in the form of full-strength plaques. Dosage from five to fifteen minutes per area often suffices. Second applications may be made four to six weeks later to eradicate missed areas or areas undertreated at the initial application. Occasionally third or fourth applications are required in instances where the lesion is more resistant

or less superficial than was estimated at the outset. Chronic indurated, long-standing lesions are probably better treated by the interstitial application of gold implants or of element needles, attacking the disease from the subcutaneous side. Here dosage may be increased to from 35 to 75 mg.-hr. per square centimeter of skin surface, employing 5 to 15 per cent of the beta rays. Second applications may be made but probably surface treatment will suffice and should be used whenever possible. Repeated interstitial applications in benign lesions are to be avoided.

Reaction. A general reaction is absent. In surface applications, locally the onset occurs from five to ten days after treatment and is characterized by an inflammatory swelling with occasional increase in scaling or crust formation which continues for two or three weeks. By the fourth week the scaling and crusting have subsided and often the paler skin surface is visible. By the fifth or sixth week the reaction is over and determination can then be made as to the result of the initial treatment and of the need for re-treatment of missed areas or those in which the lesion has not disappeared. A smooth, pale skin surface should present. Subsequent treatments, given on the surface, run practically the same course. In the case of interstitial applications, the onset is delayed to the tenth or fourteenth day and is then characterized by a subcutaneous or inflammatory swelling which goes on to disintegration and liquefaction of the involved skin areas, even to the extent of ulceration and crust formation. By the fourth or fifth week the inflammatory reaction has subsided and scaling or crusting is probably at its maximum. Separation of the crust is usually accomplished by the sixth week and the therapeutic results of the treatment are in evidence. Atrophy of the skin, fibrosis and scar formation commonly follow heavy interstitial irradiation which is justified when the induration and character of the lesion is such that beginning malignancy is suspected. Favorable cases, superficial in nature, terminate with a smooth, pale, slightly atrophic skin, free from scales and crusts. The deeper lesions terminate favorably with a deeper scar, more atrophy and increased fibrosis. Unfavorable superficial lesions recur and subsequent treatment is

indicated. Deeper seated lesions, terminating unfavorably, may degenerate into true epithelial proliferations which require heroic irradiation as do malignant growths of the nipple.

Prognosis. Practically all cases of superficial, early Paget's disease of the nipple, are completely eradicated by means of surface irradiation with light doses of beta and gamma rays. Deeper seated lesions respond equally as well when the dosage and method of irradiation are accurately adjusted to the pathology. Paget's disease proper is probably a radium case almost exclusively.

Case History

Mrs. C. Aged fifty-six. Paget's disease. Reddened, slightly corrugated thickened area 0.7 cm. in diameter. Gradual increase in size and amount of itching. Opposite breast removed six years previously for Paget's disease. Lesion present three months. Treated by 10 mg. full-strength unscreened radium plaque over windowed lead, one and three-quarters hours. Well seventeen months later.

Reference

Quigley, D. T. Discussion of papers by Drs. Kirkendall and Pfahler [Carcinoma of the Breast]: use of radium in cases of Paget's disease. *Am. J. Roentgenol.*, 8: 671, 1921.

Miscellaneous Skin Lesions (papillomata, moles, warts and corns)

Diagnosis is not discussed in this outline but should be carefully established in all instances. (See p. 13.)

Pathology. These lesions are composed chiefly of thickened hyperplastic epithelium growing in isolated areas. They are usually raised, and appear at sites of irritation, as on the sole of the foot in the case of plantar warts. The common wart may be flat or raised, acuminate or sessile; often they are multiple. Moles may be of the fleshy type, and may contain hair or pigment. Many of these lesions become painful under irritation, as is commonly true of corns and plantar warts. Irritation may change the character of moles or papillomata resulting in malignant degeneration.

Radium Indications. Radium is well fitted to remove these lesions completely. Beta rays are easily applied, the process is relatively painless and usually results in only

slight scarring, although requiring several weeks for eradication. No disability is experienced, though, cosmetically, occasionally the scar may be as undesirable as the original lesion.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Lead windows, slightly larger than the lesion and placed over it, serve to protect the surrounding tissue from the beta rays which are best administered from glazed plaques. Tubes or needles of radium element or radon may be used in lieu of plaques, proper allowance being made for the absence of soft beta rays. Full-strength glazed plaques may be used for one to one and one-half hours in superficial lesions, and four to six hours in lesions 3.0 to 5.0 mm. in thickness. Smaller windows mean relatively longer exposure because of the restricted amount of radium adjacent to the window. Plantar warts require from six to eight hours. Fleshy moles 5 mm. in thickness, require from four to eight hours. As a rule eradication should be attempted with one application. This dosage may be repeated in eight to ten weeks for missed areas or because of insufficient initial dosage. In the absence of glazed plaques, screened applicators may be used but the duration of application is longer on account of the absence of soft beta rays. Gamma rays from 10 to 25 mg. of radium are often needed to eradicate lesions 5 mm. or more in thickness, the tube being placed on top of the plaque.

Reaction. There is no general reaction to these applications. Locally, in from five to ten days the inflammatory reaction begins with a redness followed by superficial ulceration, moisture, crust, crust thickening, drying, and finally separation in from six to eight weeks. The absence of an inflammatory reaction is not uncommon in the case of corns and plantar warts. Often there is only a dryness, an increased brittleness, and a yellowish discoloration of the surface with a delayed slough *en masse*. Pain is usually negligible. The reaction to treatment of lesions about the face should be carefully considered in its relation to the cosmetic results; for although the lesion may be eradicated,

the resulting fine tissue-paper scar with occasional telangiectasis or mild pigmentation may terminate in an end result which is no more desirable then the original lesion.

Prognosis. Any superficial blemish of the skin, such as a mole, wart, or corn may be completely and permanently destroyed without marked scarring. Second and third applications occasionally are necessary but rather indicate faulty technic at the outset.

Satisfactory cosmetic results on the face are difficult to obtain and a great deal of care should be exercised before the removal of moles or papillomata of the face is attempted.

Case Histories

Mrs. B. Aged thirty-eight. Fleshy mole. Pedunculated, non-pigmented, fleshy growth in right axilla, which is tender and increasing in size. One aspect of base of lesion treated with 5 mg. full-strength plaque over windowed lead for one and one-half hrs.; then same dosage on other aspect of the base. No screen. Lesion constricted itself off in five weeks. Clinically well two and one-half years.

Mr. C. Aged forty-five. Corn. Thickened, raised, painful area on right metatarsophalangeal joint of little toe present for years. Measurement, 1.5 by 1.5 cm. and raised about 0.5 cm. Treated by 10 mg. full-strength radium plaque over windowed lead for four hours, with a screen of 0.5 mm. aluminum, totalling 40 mg.-hr. Lesion separated after two months. Clinically well, six years.

References

Ayres, S. Radium in the treatment of subungual verrucae. *Arch. Dermat. & Syph.*, 5: 748, 1922.

Pinch, A. E. H. Treatment of warts of the lips. A Report of the Work at the Radium Institute, London, Jan. 1, 1922, to Dec. 31, 1922. *Radium*, N. S., 2: 45, 1023.

Young, W. J. Verruca vulgaris treated with radium. *Urol. & Cutan. Rev.*, 26: 31, 1922.

Rodent Ulcer

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. These lesions are most commonly found on the upper part of the face, and are often called basal-celled epitheliomata. The cells are small and epithelial pearls are not seen. The degree of anaplasia is great without the usual increased degree of malignancy in proportion. The lesions are low, flat, slow growing with considerable fibrosis and subsequent central shrinking. The lesions may grow slowly for months and years, infiltrating the deep structures late

in their course. Metastasis is rare and only occurs in advanced cases. Crusted, slightly indurated edges are present. Bleeding is rare and pain usually absent.

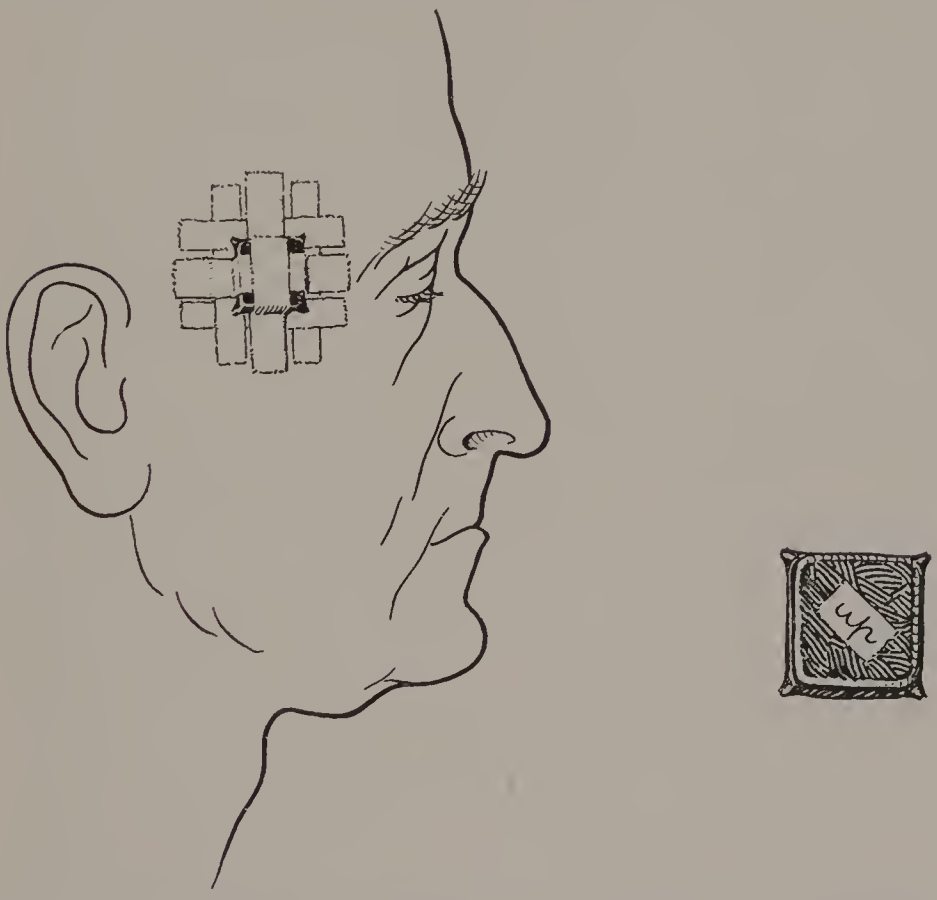


FIG. 28. Typical Radium Application in Epithelioma of Face (superficial lesion). A full strength 10 mg. radium plaque held in place by adhesive tape. Lead foil 1 mm. thick lies between plaque and skin with an open window in it slightly larger than lesion. Dosage 15 mg.-hr.

RADIUM INDICATIONS. Radium clears up practically all cases of rodent ulcer promptly, without loss of tissue and with a minimum of scarring. Radium rays cause the complete caustic necrosis of all malignant cells in superficial lesions. Rarely do rodent ulcers invade cartilaginous structures unless neglected.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. Ordinarily the full-strength glazed plaques are sufficient for the eradication of rodent ulcers. The surface method usually suffices. When the lesions are small, lead plates with windows the shape of the lesion and from 2 to 4 mm. greater in diameter, are strapped over the lesion with adhesive tape so that the whole lesion and a circlet of normal skin 2 mm. in width surrounding the lesion can be seen. The full-strength glazed plaque, covered only with thin rubber, is then strapped over the lesion. If the applicator lies flush against a raised lesion, which is not more than 2 mm. in thickness, the duration of the treatment may be from one to three hours. However, if the lesion has a crust 2 to 4 mm. thick, or if the surface is irregular and the distance from the radium to the malignant cells is increased, the duration of the application should be increased to four or six hours. In general, the dosage should be from 20 to 50 mg.-hr. per square centimeter of surface. When the induration is more than 2 mm. in thickness, it is well to reenforce the beta rays from the bare plaque by additional gamma rays from radium placed on top of the plaque, or by screening the plaque with 0.5 silver and increasing the exposure to twelve or fourteen hours at 2 to 3 mm. distance. Failures and recurrence are usually due to failure to reach the deep-lying cells which later regenerate and a recurrence results. Indurated lesions should receive from 50 to 100 mg.-hr. per square centimeter, including both beta rays from the plaque and the gamma rays from the reenforcing radium. Tubes or needles may be used in lieu of plaques by raising the tubes above the lesion by 3 or 4 mm., but not so far as to lose the beta rays which penetrate the applicator wall. Dosage must be increased according to the increase in distance. Extensive lesions require a greater irradiation at the periphery. In lesions 3.0 or more centimeters in diameter, the border may be treated in segments, often leaving the central portions to take care of themselves. Cross-fire from the irradiation of the periphery will ordinarily take care of the few weakened malignant cells which may still remain in the older central portions of the lesion. Rarely are these lesions so thick that interstitial applications are necessary or advisable. Failures

are usually due to the lack of penetration of the caustic beta rays to the deep lying malignant cells. Gamma irradiation should be used freely, better in excess than in insufficient dosage. Treatments may be repeated in six weeks to destroy recurrences or portions missed at the initial treatment. When lesions require a third treatment, it is ordinarily because they have been inaccurately treated before.

Reaction. A general reaction is absent. Locally, the lesion begins to show inflammatory changes between the fifth and tenth days. Redness, swelling, exudation of serum and crust formation succeed each other in order. By the third week the crust is well formed. The following days show the destruction and liquefaction of the deeper lying cells and the incorporation of that serum within the crust. Ordinarily the crust is dry and the redness about the periphery diminished by the fourth week. Separation of the crust follows in the fifth or sixth week, in successful cases, leaving a smooth, white scar. By the sixth week, when the crust is off, missed remnants of malignant cells can be identified as indurations or elevations about the periphery. Ulceration and persistent crusting indicate the presence of undestroyed malignant cells. If there is still doubt as to the identity of the tissue, further observation will reveal the shrinkage of scar tissue or the hypertrophy of recurrence. Re-treatment is indicated as soon as malignant tissue is identified in the lesion. The preliminary dosage may be repeated if there is recurrence at the periphery; but, if it is evident that the depth of the lesion escaped sufficient irradiation, then heavier dosage, or dosage directed more especially toward the depth should be given. Complications are few. Pyogenic secondary infection is the most common. It aids rather than hinders the eradication of the disease. Scarring is thereby often increased. Premature separation of the crust increases scarring. The fear of scar formation should not deter the radiologist from giving adequate treatment. In most instances the initial application should be the only application.

Prognosis. In rodent ulcer the prognosis is excellent. Practically all lesions are permanently healed by adequate radium treatment.

Case History

Mr. B. Aged eighty-seven. Rodent ulcer. Ulcerated lesion, 1.5 cm. in diameter on back of left hand. Searred in center. Indurated border, slightly crusted. Present six months. Treated by 10 mg. full-strength radium plaque over windowed lead, unscreened, for two and one-half hours. Clinically well nine months.

References

Johnston, L. Radium in the treatment of rodent ulcers at Sydney Hospital. *M. J. Australia*, 2: 467, 1924.

Pinch, A. E. H. Treatment of rodent ulcer of the lips. A Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, N. S., 2: 45, 1923.

Epithelioma of the Skin

Diagnosis is not discussed in this outline but should be established by biopsy in every possible instance. (See p. 13.)

Pathology. These growths are commonly of the squamous-celled type with keratinization of the older portions of the growth. They may arise anywhere that epiblastic tissue is found. The characteristics vary according to the rapidity of the growth: the slow-growing epitheliomata develop keratinization with epithelial pearls, while the rapidly growing lesions present basal-celled masses with central degeneration or necrosis. The lesions may be flat, or of a raised, exuberant nature; or infiltration and induration may be the prominent features. There is a wide variation in morphology and clinical course between the flat, slow-growing, superficial relatively non-malignant growths and those that are rapidly eroding, infiltrating and destructive with early metastases. The skin of the face is the most common site of epitheliomata, and fortunately metastasis is uncommon.

Radium Indications. The beta and gamma rays are well adapted to produce complete destruction of these superficial malignancies. These cases afford a most favorable opportunity to demonstrate the caustic action of radium. Complete necrosis of all offending cells with a minimum of injury to normal structures is almost the rule. There are few contraindications to radium in epitheliomata of the skin, with the possible exception of acute pyogenic infection which might delay the treatment.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The applications commonly employed in the treatment of epithelioma of the skin are surface, interstitial and deep external irradiation, named in the order of choice. Combinations of the three methods may be advisable in indurated or extensive lesions. Early superficial epithelioma is ordinarily best treated by bare, full-strength plaques placed against the lesion. Rubber should always be interposed between the radium and the lesion as much for mutual protection as to prevent the impinging of the very soft beta rays against the normal skin at the periphery. The very soft beta rays not infrequently produce subsequent telangiectasia which is undesirable and unnecessary. A lead plate from 0.7 to 1.0 mm. in thickness serves to protect the surrounding normal skin. An aperture or window is cut in the lead plate the shape of the lesion and in each diameter from 2 to 4 mm. larger than the lesion. The lead plate is strapped in place with adhesive tape so that the aperture exposes the entire lesion plus a narrow circlet of normal skin, thus assuring irradiation of the periphery of the lesion through the aperture. The radium applicator is strapped over the lead so that the window is covered by the flat, full-strength applicator, thus allowing the beta and gamma rays easy access to the lesion, the lead plate serving to protect the surrounding normal skin from the caustic action of the beta rays.

Superficial lesions require from forty to seventy minutes in one exposure. When the induration is thicker than 2 or 3 mm., the time of exposure should be lengthened or the beta rays may be reenforced by gamma radiation, supplied by placing radium on top of the plaque which itself screens out the beta rays.

From 50 to 200 mg.-hr. at 1.0 cm. distance usually suffices in small lesions. Employing 0.5 mm. of silver as a screen, and a distance of 3 mm., an application of 75 mg.-hr. per square centimeter in areas 4 to 5 cm. in diameter and 60 mg.-hr. per square centimeter in areas 8 cm. in diameter, constitutes adequate dosage (Quick). Much heavier irra-

diation is required for larger, thicker lesions, measuring from 2 to 4 cm. in diameter and with a thickness from 0.3 to 1.0 cm. or more. Failures are frequently due to insufficient irradiation of the depth of the lesion. Superficially they heal, but in a few weeks or months recurrences appear from undestroyed cells below the surface. When lesions are no longer superficial, interstitial applications are required for success.

Radium element needles or radon implants are most useful. From 100 to 120 mg.-hr. or mc.-hr. per cubic centimeter of malignant tissue are required. Tubes or needles, allowing the passage of 10 to 15 per cent of the beta rays may be used in lieu of plaques for surface application. Raising the applicators from 0.5 to 1.0 cm. from the surface aids in the homogeneous distribution of radiation to all parts of the lesion, giving 60 to 70 mg.-hr. per square centimeter. The milligram-hour dosage must be increased according to the square of the distance, however. The treatment of any lesion more than 2 to 3 mm. in thickness requires reenforcement from interstitial irradiation or from deep external applications, otherwise malignant cells in the depth will survive and initiate local recurrences. The dosage should be adequate. In dealing with cutaneous epitheliomata the fear of scarring should be no deterrent to adequate irradiation. Rapidly growing, extensive lesions indicate the necessity for full dosage of deep external irradiation of the draining lymphatics and neighboring lymph nodes. One thousand to 1200 mg.-hr., employing gamma rays only at 1 inch distance over each 2 sq. in. of skin surface, is ordinarily a safe skin dose. Treatments repeated day by day may be considered as one dose if given within four or five days. Applications may be repeated in four to six weeks if the reaction has subsided and the condition remains stationary or if recurrent growth is evident. Second and third applications are to be avoided if possible, but they are imperative if malignant cells are still present and actively growing.

Reaction. The reaction from radium in its destruction of the malignant tissue is easily observed clinically in cases of epithelioma of the skin. The general body reaction is not noticeable except in the extensive neglected cases which

require the administration of a large amount of irradiation at one time, a dose amounting to 5 or more gram-hours.

Locally, the reaction begins from the third to the seventh day. Redness of the skin appears about the periphery of the growth and at the same time the surface of the lesions shows moisture which dries and forms a crust. This crust thickens and elevates until the disintegration of cells ceases. The crust continues to increase for perhaps three weeks or even longer. The redness about the lesions increases to a flaming red, remains stationary for a while, and then fades so that by the fourth week, or at the latest the fifth, the redness has subsided and the drying crust shows signs of separation. Incomplete destruction with recurrence at the site within a few weeks is not uncommon, but on second application more vigorous and deeper irradiation usually disposes of the lesion permanently. Extensive lesions with metastases in lymph nodes render the prognosis desperate, and heroic measures must be instituted. Rapidly growing lesions with metastases are rarely cured, but palliation and inhibition of progress are accomplished. In successful cases, the crust separates normally as soon as the epithelium has covered the underlying ulcer. A smooth, depressed, white, tissue-paper scar marks the site of the lesion if treatment has been adequate. The total period of reaction and healing varies from four to six weeks. Extensive cases in which massive necrosis is produced by heavy irradiation may slough and discharge serum and fragments of necrotic material for six to eight weeks, gradually healing from the margin as the sloughing is completed. When the necrosis is extensive and the discharge profuse, daily dressings are required. Mild antiseptics and deodorants are indicated, such as boric acid solution, potassium permanganate or peroxide. Sloughs should be allowed to disintegrate and separate spontaneously. No local application seems to hasten the process of sloughing and repair. Smaller lesions are best left open to the air to dry and crust spontaneously. Should there be incomplete destruction of the lesion, recurrence will be manifested as early as the fifth week. Regrowth indicates immediate renewed irradiation. Complications are rare, cellulitis being only occasionally encountered.

Prognosis. Radium produces clinical cure in practically all epitheliomata of the skin unless extensive. Involvement of bone or cartilage renders the prognosis grave.

Case History

Mr. S. Aged thirty-nine. Epithelioma of skin. Flat, crusted, slightly raised, indurated lesion 1 cm. diameter on right temporal region., 2 mm. thick. Appears actively growing. Duration, eight weeks. Treated by 35 mg. of radium (10 mg. in full-strength plaque, unscreened, over windowed lead, with 25 mg. on top of plaque) for two hours, totaling 70 mg.-hr. Clinically well eleven months.

References

Allen, B. Squamous-celled epithelioma responding to roentgen and radium therapy. *J. Roentgenol.*, 1: 264, 1918.

Boggs, R. H. The treatment of epithelioma by radium. *Radium*, N. S., 1: 113, 1922.

Bordier, H. Multiple roentgen epitheliomas cured by diathermy. *Bull. de l'Acad. de méd.*, 88: 248, 1922.

Bowen, C. F. Superficial malignancies. *Ohio State M. J.*, 18: 60, 1922.

Brock, W. What conditions determine the roentgenotherapy of epithelial cancer? *Strahlentherapie*, 13: 1, 1921–22.

Clark, A. S. Radium treatment of cutaneous epitheliomas by single or massive doses. *J. A. M. A.*, 62: 1453, 1914.

Cole, A. M. The use of x-ray and radium in superficial malignancies. *J. Indiana M. A.*, 17: 71, 1924.

Daland, E. M. End-results of radium treatment of skin cancer. *J. A. M. A.*, 86: 471, 1926.

Duncan, R. Superficial epitheliomas with results and observations in the treatment of more than 500 cases with radium. *Urol. & Cutan. Rev.*, 26: 19, 1922.

Duncan, R., and Ward, E. D. The grading of epitheliomas and their radiation sensibility. *N. York M. J.*, 118: 681, 1923.

Engman, M. F., and Kimbrough, J. S. Radium in the treatment of basal celled cancer. *Urol. & Cutan. Rev.*, 23: 1, 1919.

Gilchrist, T. C. Cancer of the skin. *Maryland M. J.*, 58: 157, 1915.

Hazen, H. H. Lessons learned from failures in the roentgen-ray treatment of cutaneous cancer. *J. Cancer Research*, 9: 404, 1925.

James, W. D. and James, A. W. Epitheliomata—prophylactic and curative measures. *Internat. J. Surg.*, 36: 109, 1923.

Josselyn, R. B. Radiotherapy in the treatment of superficial malignant disease. *Urol. & Cutan. Rev.*, 28: 270, 1924.

Kennedy, T. C. Radium treatment of epithelioma. *J. Indiana M. A.*, 9: 298, 1916.

KENNEDY, W. H. Cornifying carcinoma of the skin treated with radium. *Urol. & Cutan. Rev.*, 26: 557, 1922.

KENNEDY, W. H. Radium treatment of epithelioma of the face. *J. Radiol.*, 6: 52, 1925.

MACNEAL, W. J., and WILLIS, G. S. A skin cancer following exposure to radium. *J. A. M. A.*, 80: 466, 1923.

DE MARTEL, T. Epithelioma developing from a nevus, operated on four times, treated by x-rays and radium, with recurrence each time, cured after five months, by fulgurations according to Keating-Hart's method. *Bull. et Mem. Soc. de chir. de Paris*, 47: 1185, 1921.

MORROW, H., and TAUSSIG, L. Epitheliomas of the face and their treatment with radium. *Arch. Dermat. & Syph.*, N. S. 5: 73, 1922.

MORROW, H., and TAUSSIG, L. Statistics and technic in the treatment of malignant disease of the skin by radiation. *Am. J. Roentgenol.*, 10: 212, 1923.

MORTON, J. J. Cancer of the skin. *Arch. Surg.*, 12: 655, 1926.

NEELY, S. D. Combination of x-ray and radium therapy in the treatment of superficial malignancies of the face. *J. Oklahoma M. A.*, 16: 212, 1923.

PARES. Curietherapy of spindle cell epithelioma of the skin. *J. de radiol. et d'électrol.*, 6: 487, 1922.

PFAHLER, G. E. The treatment of skin cancer by x-rays, radium and electrocoagulation. *N. York M. J.*, 116: 553, 1922.

PENDERGRASS, E. P., and RAVDIN, I. S. A report of two cases of malignancy in xeroderma pigmentosum and their response to radium. *Urol. & Cutan. Rev.*, 27: 207, 1923.

QUIGLEY, D. T. The treatment of superficial cancer. *Am. J. Roentgenol.*, 10: 161, 1923.

REGAUD, C. The principles of radiotherapy of epidermoid epitheliomas and its application to epidermoids of the skin and mouth. *J. de radiol. et d'électrol.*, 7: 297,1923.

SIMMONS, C. C. Radium treatment of carcinoma of the skin. *Boston M. & S. J.*, 181: 477, 1919.

SIMPSON, F. E. Radium in the treatment of cancer and various other diseases of the skin. *J. A. M. A.*, 67: 1508, 1916.

STEVENS, R. H. The radiologic treatment of superficial cancer. *Urol. & Cutan. Rev.*, 26: 34, 1922.

STEVENS, J. T. Statistics and technic in the treatment of superficial malignancy with radium. *Am. J. Roentgenol.*, 11: 241, 1924.

SWEITZER, S. E. An analysis of forty-three cases of skin cancer. *J. A. M. A.*, 69: 179, 1917.

TAFT, R. Radiotherapeutics in skin cancer. *Urol. & Cutan. Rev.*, 26: 55, 1922.

DE VERTEUIL, F. L. Notes on a case of epithelioma treated by radium. *Radium*, 3: 23, 1914.

WASSINK, W. F. et al. Results of radiation treatment of skin carcinoma. *Acta Radiol.*, 4: 146, 1925.

WITHERS, S., and RANSON, J. R. The treatment of malignant growths about the face. *Colorado Med.*, 21: 92, 1924.

Pruritus Ani and Pruritus Vulvae

Diagnosis is not discussed in this outline but should be established by all reasonable means. (See p. 13.)

Pathology. Often no demonstrable pathology can be found; at least there is nothing pathognomonic. Secondary excoriations, crusting and scar formation may be present from irritations of all sorts. Possibly the lesion is located in the nerve endings.

Radium Indications. Radium rays have proved of value in a fair proportion of cases. It is not regularly dependable, but it offers the only method of relief in many cases and the best in a fair proportion of them. Its use is advisable when other ordinary measures have failed.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Application. The beta or gamma rays may be employed in the treatment of these lesions. If the beta rays are to be depended upon, full-strength glazed plaques, covered with rubber only, may be applied for fifteen to thirty minutes per area. Anal and vulvar folds should be flattened out by tension so that all the involved skin may receive adequate dosage. Gamma rays may be used to reenforce the beta radiation in order to reach the depths of the folds. The gamma ray alone may be used with a dosage kept below the dose which will cause ulceration. The erythema dose seems to yield the best results. Two hundred millgram-hours at 1.25 cm. distance, over each 2 sq. in. of surface, is an average dose. This may be given in divided doses, three to four days apart. Repetition of the dose may be administered in four to six months.

Reaction. There is no general reaction. Locally a slight erythema begins in five to ten days with the occasional appearance of moisture, especially if the surface was excoriated at the outset. The pruritus may be relieved within two days or it may be increased during the period of the erythema. Pruritus often persists until the inflammatory reaction has subsided. The end result is usually a marked relief from the pruritus, and in many cases complete cure.

A certain proportion of cases seem to be unaffected or but little influenced by radiation. None seems to have been made worse.

PROGNOSIS. Radium offers a fair chance of relief in these intractable conditions. A few patients experience complete and permanent relief. The majority improve and may be re-treated with benefit. A minority of the cases are unimproved.

PSORIASIS

Diagnosis is not discussed in this outline, but should be established by careful study. (See p. 13.)

PATHOLOGY. Psoriasis is a chronic inflammatory process of the skin, characterized by a redness which is present on a raised area, caused by an increase in the epithelium of the corium. The surface presents a dry scale having a pearly appearance. These lesions may be distributed over the whole body in large sheets or in many scattered isolated areas. Pruritus is not an uncommom symptom. These lesions may recur at intervals over any portion of the whole surface of the body.

RADIUM INDICATIONS. It is better to employ chiefly the beta rays to induce the regression of these lesions. They are of easy access for treatment and observation. No inflammatory reaction is required except in the deep-seated chronic lesions, or those occurring under the nails or in folds of the skin. The exposures are short, so that fairly extensive lesions can be readily treated. Radium is of special value in the relief of the pruritus. Only instances of relatively small, isolated patches of psoriasis are suitable for radium treatment; generalized or extensive lesions are commonly treated with roentgen ray or other measures.

The *contraindications* and *dangers* of radium therapy are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. Surface applications, employing full-strength glazed plaques are well adapted for the treatment of these lesions. Rubber covered plaques applied from three to ten minutes per area suffice in the superficial types. The inflammatory reaction should be avoided. Application may

be repeated in ten to twenty days or more often if the therapeutic dosage is kept well below the erythema dose. Thicker lesions require screens of 0.1 to 0.2 mm. of lead. Deep-seated lesions require the harder beta and gamma rays. Screening of 0.5 mm. of silver or more with the distance of ¼ inch, employing 100 to 200 mg.-hr. per 2 sq. in. seems most efficient.

Reaction. There is no general reaction in the treatment of psoriasis. Locally, there is no inflammatory reaction if the duration of the treatment is gradually increased to the point where the therapeutic dose is demonstrated to be below that of the erythema dose. The scaling decreases, the redness disappears, the lesion flattens, and gradually fades to normal. The local inflammatory reaction, if obtained, goes through redness, scaling, and crusting, in the order named during a period of from two to four weeks. Scarring may result. The lesions may recur at the site or elsewhere on the body within a few months or years. In practically all instances the pruritus associated with some of these lesions is readily relieved.

Prognosis. The results obtained by the use of radium in psoriasis are good in most instances. Deep-seated lesions require the use of gamma rays, and the results are obtained more slowly. Pruritus is relieved within a few days. Recurrences are likely. In general, radium therapy is suitable for psoriasis.

Ringworm (tinea favosa, tonsurans, and sycosis)

Diagnosis is not discussed in this outline but should be established by laboratory examination in every possible instance. (See p. 13.)

Pathology. Ringworm is a chronic, non-limited inflammation of the skin of the scalp, the bearded face, or the hairless skin. The causative factor is a mold which gains a foothold in the hair follicles and causes a chronic inflammatory process which is frequently accompanied by secondary infection.

Radium Indications. The desideratum in the treatment of these lesions is to produce an epilation, temporary in nature. Radium rays are capable of producing temporary

epilation with but little visible, local reaction or general disturbance. The lesions are of easy access for treatment and observation. The application once determined upon, is simply made. However, the complete epilation with radium of any area more than 1.0 or 2.0 cm. in diameter is to be attempted only by the expert in radium therapy.

Application. The whole area involved must be epilated. The dosage varies with screening and distance. Gamma rays at one inch distance to the extent of 1200 mg.-hr. will epilate temporarily about 3 sq. in. of skin area. Twenty milligram-hours per square centimeter are required with distance of 0.5 cm. and a screen of 1.0 mm. of aluminum; at a distance of 2.0 cm. with 2.0 mm. of brass the dosage should be 56 mg.-hr. (Mazzoni and Palumbo; Frank Simpson.)

The epilating dose and its application are best worked out by the individual radiologist according to the amount of radium available and the exigencies of the case at hand. Erythema or local normal skin reaction is to be avoided. When large areas are irradiated, the dosage had best be given in divided applications, providing all exposures are given within ten days. When the total dosage reaches 4 or 5 gm.-hr., there may be a marked general reaction. Divided dosage tends to prevent such reaction.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

Reaction. There is no general reaction unless heavy irradiation is given at one sitting. Locally, the hair falls out in from fourteen to twenty days. Careful irradiation results in no local inflammatory process. The hair returns within three months. Epilation effects a cure.

Prognosis. The results are excellent when careful, complete temporary epilation is accomplished. Radium is especially siutable for small, isolated areas or multiple small foci.

Case History

Mr. F. Aged forty-two. Ringworm of leg. Inflamed, slightly raised, punctate, itching patch on right anterior aspect of leg. Clinical diagnosis: ringworm.

Treated by 100 mg. of radium, employing 13 per cent of beta rays, for thirty minutes, totalling 50 mg.-hr. Clinically well two years.

REFERENCE

MAZZONI, L., and PALUMBO, V. Treatment of ringworm with radium. *Policlinico*, sez. prat., 28: 503, 1921.

TUBERCULOUS ULCERS AND SINUSES

Diagnosis is not discussed in this outline but should be established by careful laboratory tests in every possible instance. (See p. 13.)

PATHOLOGY. The tuberculous process in these lesions is subcutaneous in origin, most frequently arising about lymph nodes. There is a breaking-down of the skin, with ulceration, protracted healing, and not uncommomly burrowing of the ulceration to form sinuses. These lesions are not unlike scrofuloderma which is not so common as formerly. General hygienic and local measures have decreased its incidence. Well established ulcers and sinuses of tuberculous nature do not heal readily.

RADIUM INDICATIONS. Moderately stimulating doses of beta and gamma rays from radium in most instances cause these ulcers and sinuses to heal rapidly with but little reaction. The dosage is small and easy of application, and observation of the lesion is simple. Fever is not an absolute contraindication but indicates caution.

The *contraindications* and *dangers* of radium treatment are discussed under those general headings and should be carefully studied before the radium is used. (See p. 15.)

APPLICATION. Ulcers may be treated with full strength glazed plaques or with tubes of radium element in doses of fifteen to thirty minutes of unscreened rays or thirty to sixty minutes employing 0.5 mm. of silver and rubber. These dosages should be applied to each 2 sq. cm. of surface. In the case of sinuses, tubes may be employed to the extent of 10 mg.-hr. per 2.0 cm. of linear measure, employing a screen of 0.5 mm. of silver and rubber. If the lumen of the sinus is larger, the depth should be explored with a sound and a radiferous tube inserted on a flexible wire to the depth, withdrawing 2.0 cm. per hour if a 10 mg. tube is used. In

the case of deep sinuses, it is probably best to irradiate only the 6.0 cm. at the depth at one sitting. This method tends to prevent healing near the mouth of the sinus, thus pinching off a portion of the depth, leaving opportunity for the formation of cold abscess. The dosage may be repeated in from four to six weeks, as indicated by incompletely healed lesions or inaccurate irradiation at the time of the initial dose.

Reaction. There is no general reaction except in deep extensive sinuses with cavity formation and retained secretion. Instances of perirenal or psoas abscesses may be mentioned as examples in which marked general reaction may be obtained. In the presence of marked general lowered resistance, the dosage should be kept small, under 50 mg.-hr. every three days. Free, open drainage of sinuses is essential to proper therapy. Dosage should be kept small, given in divided amounts, when fever is present. Careful clinical observation, day by day, is imperative in such lesions. Locally, the reaction consists of a slight inflammation with increased discharge. The reaction begins within three to five days. The discharge is profuse for a week, gradually decreasing, and is accompanied by the healing of the sinus from the depth. In ulcers the reaction begins from three to five days with an inflammatory swelling and increased moisture which subsides by drying, with crust formation and eventually healing. The reaction is over in from four to five weeks. In successful cases, complete healing occurs with but slight scar formation. Sinuses may heal 2.0 to 4.0 cm. from the depth in six weeks. No further treatment is indicated as long as healing from the bottom is in progress.

Prognosis. Superficial ulcers and narrow sinuses heal readily in most instances. Sinuses with deep branchings of large lumen and cavity formation heal with difficulty, and much of the success depends upon the anatomic structures forming the walls of the sinuses. Bony or cartilaginous walls heal with great difficulty. Patient, conservative irradiation, in a patient with good vital resistance, may accomplish much in the healing of extensive tuberculous sinuses.

Case History

Mr. C. Aged thirty. Tuberculous ulcer. Indolent, slightly crusted area on back of hand, present for two years. Not indurated. Clinical diagnosis: tuberculous ulcer. Treated by 100 mg. of radium, 6.0 mm. distance, with beta ray screen over whole area, in doses divided over seven days' time. Markedly improved in one month. Granulating. Clinically well five years.

References

Krull, C. A. Radiotherapy of ocular tuberculosis. *Nederl. Tijdschr. v. Geneesk.*, 1: 630, 1923.

Pfahler, G. E., and Widmann, B. P. Case of tuberculous gingivitis treated with apparent success by radium. *Am. J. Roentgenol.*, 9: 756, 1922.

Southard, J. D. Radiotherapy in the treatment of bone tuberculosis and other conditions. *J. Arkansas M. Soc.*, 20: 6, 1923.

Wassing, H. Radium therapy of tuberculous eye lesions. *Klin. Monatsbl. f. Augenhlk.*, 72: 175, 1924.

SUPPLEMENTARY BIBLIOGRAPHY

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General Considerations

Abbé, R. The therapeutics of radium. *Canad. Pract. & Rev.*, 39: 197, 1914.

Abbé, R. The use of radium in malignant disease. *Lancet*, 2: 524, 1913.

Abbé, R. Radium efficiency in non-malignant surgical conditions. *Med. Rec.* 90: 47, 1916.

Aikins, W. H. B., and Simon, K. M. B. The histological and clinical changes induced by radium in carcinoma and sarcoma. *Dominion Med. Monthly*, 43: 97, 1914.

Allen, E. V., Bowing, H. H., and Rowntree, L. G. The use of radium in internal medicine; further experiences. *J. A. M. A.*, 88: 164, 1927.

Bardeen, C. R. Biological effects of roentgen and gamma rays. *Wisconsin M. J.*, 25: 215, 1926.

Bayet, A. General principles of radium-surgery. *Brit. J. Radiol.*, 30: 368, 1925.

Beck, E. G. Cancer therapy from the surgeon's standpoint. *Am. J. Roentgenol.*, 11: 117, 1924.

Beck, E. G. Clinical demonstration of apparently hopeless cases of cancer treated by surgery and radium. *Internat. Clin.*, 1: 122, 1922.

Béclère. A. Radiosensitivity of neoplastic cells. *Strahlentherapie*, 23: 9, 1926; *Acta radiol.*, 6: 141, 1926.

Bissell, J. B. Cancer and radium. *Internat. J. Surg.*, 27: 182, 1914.

Bissell, J. B. Some radium therapeutics. *Med. Rec.*, 86: 55, 1914.

Bissell, J. B. Radium therapeutics otherwise than for malignancy. *Med. Rec.*, 87: 1023, 1915.

Bissell, J. B. Cancer destruction by radium. *Surg., Gynec. & Obst.*, 21: 98, 1915.

Bissell, J. B. Radium in various surgical conditions. *New York State J. M.*, 16: 590, 1916.

Bissell, J. B. Special radium needles in use at the radium sanitarium of New York. *Am. Med.*, 11: 520, 1916.

Boggs, R. H. The local application of radium supplemented by roentgen therapy. *Surg. Gynec. & Obst.*, 22: 358, 1916.

Boggs, R. H. Radium and deep therapy in the treatment of malignancy. *Radium*, 18: 49, 1921–22.

Bowing, H. H. Topical applications of radium. *Am. J. Roentgenol.*, 7: 582, 1920.

Brulé, M., and Boulin, R. Pernicious anemia due to radium. *Bull. et mém. Soc. méd. d. hôp. de Par.*, 49: 528, 1925.

Bruzau and Ferroux. Principles and methods of distant radium therapy. *Cancer Bruxelles*, 4: 146, 1927.

Bryant, F. Malignancy and radiation; a study of the relation of the structure of cancer tissue to radiation. *Boston M. & S. J.*, 182: 263, 1920.

Bumm, E. Results of roentgen ray and mesothorium treatment in carcinoma of the uterus. *Berl. klin. Wchnschr.*, 50: 1001, 1913.

Burnam, C. F. A brief outline of the status of radium therapeutics. *Johns Hopkins Hosp. Bull.*, 26: 190, 1915.

Burns, F. S. Radium in the treatment of non-malignant diseases of the skin. *Boston M. & S. J.*, 191: 16, 1924.

Burrows, A. A report of the work at the Manchester and district radium institute, Jan. 1, 1921 to Dec. 31, 1921. *Radium*, 1: 149, 1922.

Butts, D. C. A. Outstanding physical considerations in radium and roentgen therapy. *Radiology*, 6: 47, 1926.

Cameron, W. H. Easy method for making surface casts to hold radium tubes in position. *Radiology*, 8: 438, 1927.

Cameron, W. H. Classification of the various methods employed in the internal administration of radium emanation and radium salts. *Radium*, 4: 57, 1915.

Carneiro, F. J. and Martins, T. Radioactivity and oligodynamic action of metals. *Compt. rend. Soc. de biol.*, 95: 1498, 1926.

Charlton, C. J. Biological effect of radium. *Radiology*, 7: 137, 1926.

Clark, J. J. The combined use of x-ray and radium in the treatment of malignant disease. *J. M. A. Georgia*, 10: 839, 1921.

Clark, W. L. The rôle of radium needles in the treatment of neoplastic diseases. *Am. J. Roentgenol.* 10: 204, 1923.

Coliez, R. Technics for telecurietherapy. *J. de radiol. et d'électrol.*, 11: 581, 1927.

Collin, E. Radiotherapy as applied at the Pasteur institute. *Ugesk. f. Laeger*, 84: 1247, 1922.

Delano, S. A study in the internal therapeutics of radium. *Med. Rec.*, 88: 137, 1915.

Discovery of radium. *Arch. Physical Therapy*, 7: 100, 1926.

Duane, W. Methods of preparing and using radioactive substances in the treatment of malignant disease and of estimating suitable dosages. *Boston M. & S. J.*, 177: 787, 1917.

Enfield, C. D. Some fundamental considerations in radium and roentgen ray therapy. *Am. J. Surg.*, 38: 302, 1924.

Esdra, C. Ten years of radiotherapy. *Policlin.*, 22: sez. prat., 449, 1915.

Ewing, J. Tissue reactions to radiation. *Am. J. Roentgenol.*, 15: 93, 1926.

Ewing, J. Influence of radium on cancer tissues. *Am. J. Roentgenol.*, 5: 413, 1918.

Fabry, J. Pathogenesis and treatment of superficial angiectases after irradiation with roentgen, radium, and mesothorium. *Med. Klin.*, 22: 1408, 1926.

Failla, G. Discussion of Dr. Janeway's doses for buried emanation. *Am. J. Roentgenol.*, 7: 334, 1920.

Failla, G. Dosage in radium therapy. *Am. J. Roentgenol.*, 8: 674, 1921.

Failla, G. A new method of intratumoral irradiation. *Brit. J. Radiol.*, 30: 420, 1925.

Failla, G. The development of filtered radon implants. *Am. J. Roentgenol.*, 16: 507, 1926.

Failla, G. Biological unit of radiation. *Acta radiol.*, 6: 413, 1926.

Failla, G. Design of well-protected radium "pack." *Am. J. Roentgenol.* 20: 128, 1928.

FISCHEL, E. Radium and internal medicine. *Ann. Clin. Med.*, 3: 245, 1924.
FISCHER, R. Treatment and radioscopy with radium. *Néoplasmes*, 6: 84, 1927
FOOTE, E. M. The place of radium in surgery. *Ann. Surg.*, 65: 273, 1917.
FREUND, L. Experiences with radium and mesothorium. *Wien. klin. Wchnschr.*, 26: 393, 1913.
FRIEDRICH, W. Physical bases for radium therapy. *Fortschr. a. d. Geb. d. Roentgenstrahlen* (Kongresshft.), 36: 57, 1927; *Strahlentherapie*, 26: 4, 1927.
GAARENSTROOM, G. F. Radiotherapy of cancer. *Nederl. Tijdschr. f. Geneesk.*, 65: pt. 2, 2480, 1921.
GAGEY, J. The rational distribution of radium for a hospital service. *J. de radiol. et d'électrol.*, 7: 182, 1923.
GOODMAN, H. History of radium in dermatology. *M. Life*, 34: 539, 1927.
GOTTESMAN, J., and BENDICK, A. J. Pneumopericardium from radium necrosis. *Am. J. M. Sc.*, 171: 715, 1926.
GRAHAM, J. C. General consideration of radiotherapy. *Long Island M. J.*, 16: 328, 1922.
GREENOUGH, R. B. The treatment of malignant diseases with radium and x-ray. *Surg., Gynec. & Obst.*, 39: 18, 1924.
GRIER, G. W. The radiation treatment of malignancy. *Am. J. Roentgenol.*, 15: 436, 1926.
GUY, W. H., and JACOB, F. M. Some comments on radium technique. *Atlantic M. J.*, 26: 453, 1923.
HAGGARD, W. D., and CRUTCHFELD, C. E. Radium therapy. *J. Tennessee M. A.*, 14: 423, 1922.
D'HALLUIN, M. Cure of cancer several years after treatment with radium. *Arch. d'électric méd.*, 34: 97, 1924.
HANDLEY, W. S. The encirclement method of using buried radium tubes. *Brit. J. Radiol.*, 30: 422, 1925.
HARTMANN. Case of bone necrosis from radium therapy. *Rev. gén. de clin. et de thérap.*, 41: 152, 1927.
HOFFMAN, F. L. Progress and results in cancer control. *Boston M. & S. J.*, 188: 221, 1923.
HOLDING, A. F., and LONG, W. B. The truth about radioactive therapy in malignant growths. *J. A. M. A.*, 59: 982, 1917.
HOLDING, A. F. Cancer ameliorations and cancer immunity. *Am. J. Roentgenol.*, 7: 306, 1920.
JANEWAY, H. H. The use of buried emanation in the treatment of malignant tumors. *Am. J. Roentgenol.*, 7: 325, 1920.
JANSEN, H., and SCHULTZER, P. Internal radium emanation therapy; emanatorium experiments with rats. *Acta radiol.*, 6: 631, 1926.
JONES, A. P. How does radium produce its results? *Virginia M. Monthly*, 50: 768, 1924.
KAYE, G. W. C. Radiology and physics. *Arch. Radiol. & Electroth.*, 26: 336, 1922.
KENNEDY, T. C. The present status of radium therapy. *J. Indiana M. A.*, 12: 36, 1919.

KING, H. Three years' experience with radium. *J. Tennessee M. A.*, 16: 292, 1923.

KIRKENDALL, B. R. Pre-operative and post-operative radium therapy. *Ohio State M. J.*, 17: 837, 1921.

KLEIN, G. The quantitative expression of dosage in radium and mesothorium therapy. *München. med. Wchnschr.*, 61: 661, 1914.

KLEWITZ. Radiotherapy of malignant tumors in internal medicine. *Deutsche med. Wchnschr.*, 50: 399, 1924.

KNOX, R. Problems in radiotherapy. *Arch. Radiol. & Electroth.*, 27: 69, 1922.

KRAPH, E. F. Recent investigations on the use of radium for malignant diseases. *Radium*, 1: No. 2, p. 10, 1913.

KRÖNIG and GAUSS. The treatment of cancer with roentgen rays and mesothorium. *Deutsche med. Wchnschr.*, 39: 1233, 1913.

KUMER, L. The management of roentgen and radium ulcers. *München. med. Wchnschr.*, 68: 1084, 1921.

KUMER, L. Apparatus for introduction of radium tubes in filter. *Strahlentherapie*, 23: 184, 1926.

KURTZAHN. Radiotherapy of malignant neoplasms in surgery. *Deutsche med. Wchnschr.*, 50: 394, 1924.

LABORDE, S. Radium therapy of cancer. *Arch. Radiol. & Electroth.*, 27: 114, 1922.

LACAPÉRE, G. The action of radium depends upon quantity and duration of treatment. *Brux.-Méd.*, 7: 22, 1926.

LAIN, E. S. The present status of radium therapy. *South. M. J.*, 15: 495, 1922.

LAZARUS, P. Therapeutic use of radiothorium. *Deutsche med. Wchnschr.*, 48: 451, 1922.

LEITCH, A. Radium. *Journal-Lancet*, 42: 9, 1922.

LEVIN, I. The relative value of surgery, radium and x-rays in cancer therapy. *Urol. & Cutan. Rev.*, 26: 5, 1922.

LEVIN, I. Morphologic appearance of cancer clinically cured by radium and roentgen ray. *J. A. M. A.*, 69: 1068, 1917.

LOMHOLT, S. Radioactive substances in fluid form. *Hospitalstid.*, 65: 865, 1922.

LOUCKS, R. E. Indications for radium therapy in ophtho-oto-laryngology. *J. Michigan, M. Soc.*, 22: 63, 1923.

MACDONALD, C. The principles underlying treatment by radium. *M. J. Australia*, 1: 398, 1927.

MACKAY, H. The anchoring of radium needles. *Canad. Pract.*, 48: 337, 1923.

MALLET, L., and COLIEZ, R. Technique of deep curietherapy at great distance and crossed fire on separate fields and localities. *Bull. Acad. de méd., Par.*, 93: 146, 1925.

MALLET, L. and COLIEZ, R. Investigations in distribution of radiant energy in radium therapy: direct measurement of gamma radiation. *Strahlentherapie*, 22: 417, 1926.

MALLET, L., and COLIEZ, R. Diffusion of radium rays in surface applications. *J. de radiol. et d'électrol.*, 10: 551, 1926.

MATAS, R. Radium therapy. *Am. J. Roentgenol.*, 7: 440, 1920.

MAYER, L., and CHEVAL, M. Technic of deep radium therapy. *Brux.-méd.*, 7: 452, 1927.

MAYER, L., and CHEVAL, M. Deep radium therapy; methods, diagrams and illustrations. *Actinoterapia*, 6: 137, 1927.

MAYO, W. J. The relation of cancer to the prolongation of human life. *Surg., Gynec. & Obst.*, 30: 22, 1920.

MAZERES, M. Primary gamma radiation around linear radium source. *J. de radiol. et d'électrol.*, 10: 159, 1926.

MORAN, H. M. The problem of malignant disease. *M. J. Australia*, 1:632, 1923.

MORTON, W. J. Imbedded radium tubes in the treatment of cancer, with report of a case of sarcoma remaining cured nine years after radiation. *Med. Rec.*, 86: 913, 1914.

MOTTRAM, J. C. Early changes in nucleus of cells of tumours following exposure to beta radiations. *Brit. J. Radiol.*, 32: 61, 1927.

MUIR, J. Radio-active substances and their therapeutic uses and applications. *Radiology*, 4: 40, 1925; 6: 41; 146; 246; 310; 419; 509, 1926; 7: 51; 131; 242; 332; 426; 507, 1926; 8: 34; 127; 223; 330; 416, 1927.

MÜLLER, E. Blood pressure reducing effect of radium baths and radium emanation. *Klin. Wchnschr.*, 4: 2477, 1925.

NEWCOMET, W. S. Radium and roentgen rays in radiotherapy, their uses and limitations. *J. A. M. A.*, 63: 743, 1914.

NEWCOMET, W. S. A comparison of the uses of the roentgen ray and of radium, with lantern demonstrations. *Penn. M. J.*, 18: 136, 1914–15.

NEWCOMET, W. S. The use of roentgen and radium rays in medicine. *Urol. & Cutan. Rev.*, 26: 1, 1922.

NEWELL, E. D. Conclusions after six years' use of radium. *South. M. J.*, 16: 706, 1923.

NOGIER, T. Marked augmentation of the action of radium and roentgen rays in the treatment of neoplasms. *Arch. d'électric. med., etc.*, 4: 114, 1924.

NORSWORTHY, O. L. Instrument for introducing needles of radium salts. *Am. J. Roentgenol.*, 15: 174, 1926.

OPITZ, E. The dosage and therapeutic effect of roentgen and radium rays. *Arch. f. Gynäk.*, 117: 223, 1922.

OPITZ, E. Principles of radiotherapy of carcinomas. *Am. J. Roentgenol.* 10: 312, 1923.

OPITZ, E. The biology of radiotherapy of cancer. *Strahlentherapie*, 15:750, 1923.

PALVARINI, A. Radium therapy. *Radiol. med.*, 12: 709, 1925.

PFAHLER, G. E. Malignant disease and its treatment by the x-rays, radium and electrocoagulation. *Northwest Med.*, 22: 432, 1923.

PFAHLER, G. E. Radiation therapy in deep seated malignant disease. *Surg., Gynec. & Obst.*, 41: 443, 1925.

PFAHLER, G. E. Radium applications in certain cases of carcinoma. *Am. J. Roentgenol.*, 17: 361, 1927.

PIERSALL, C. E. Present-day x-ray and radium therapy. *California State J. M.*, 22: 9, 1924.

PILGER, W. Radium in the treatment of cancer. *J. Cancer*, 1: 90, 1924.

PINCH, A. E. H. A report of the work carried out at the Radium Institute, London, in 1914. *Brit. M. J.*, 1: 367, 1915.

PINCH, A. E. H. A report of the work carried out at the Radium Institute, London. Annual report for 1918. *Radium*, 13: 49; 65, 1919.

PINCH, A. E. H. A report of work carried out at the Radium Institute, London. Annual report for 1919. *Radium*, 15: 69; 85, 1920.

PINCH, A. E. H. Report of the work carried out at the Radium Institute, London, from Jan. 1, 1921 to Dec. 31, 1921. *Radium*, 1: 124, 1922.

PINCH, A. E. H. A report of the work carried out at the Radium Institute, London, from Jan. 1, 1922 to Dec. 31, 1922. *Radium*, 2: 39, 1923.

PINCH, A. E. H. A report of the work carried out at the Radium Institute, London, Jan. 1, 1923 to Dec. 31, 1923. *Radium*, 3: 1, 1924.

PINCH, A. E. H. Adenomata, Villous Tumors and Polypi of the Rectum. A report of the work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922, *Radium*, 2: 59, 1923.

PIRIE, A. H. A fundamental principle for the curative action of radium and x-rays. *Urol. & Cutan. Rev.*, 28: 289, 1924.

PISTON, D. S. Graphical methods of calculation in radium therapy. *Am. J. Roentgenol.* 15: 451, 1926.

POMEROY, L. A. Indications for radium treatment. *Ohio State M. J.*, 19: 324, 1923.

PROESCHER, F. The intravenous injection of soluble radium salts in man. *Radium*, 1: 9, 1913.

PROESCHER, F. The intravenous injection of soluble radium salts. *Radium*, 2: 61, 1914.

PROESCHER, F., and ALMQUEST, B. R. Contribution on the biological and pathological action of soluble radium salts. *Radium*, 3: 65, 1914.

QUICK, D. A. The value of interstitial radiation. *Am. J. Roentgenol.*, 9: 161, 1922.

QUICK, D. The response of various types of cancer to radium. *Canad. Pract.*, 48: 1, 1923.

QUICK, D. The radium in adequate dosage in the treatment of cancer. *J. A. M. A.*, 89: 2035, 1927.

QUIGLEY, D. T. The technique of radium application. *Minnesota Med.*, 2: 97, 1919.

QUIMBY, E. H. Method for study of scattered and secondary radiation in x-ray and radium laboratories. *Radiology*, 7: 211, 1926.

QUIMBY, E. H. Intensity of radiation in vicinity of filtered radon implants. *Radiology*, 10: 365, 1928.

RÉCHOU, G. Present technique of radium therapy. *J. de radiol. et d'électrol.*, 10: 359, 1926.

REGAUD, C. General principles applicable in the treatment of cancer. *Arch. d'électric. méd. etc.*, 31: 63, 1921.

REITTER, G. S., and MARTLAND, H. S. Leukopenic anemia of regenerative type due to exposure to radium and mesothorium; report of case. *Am. J. Roentgenol.*, 16: 161, 1926.

RICHARDS, T. W., and LEMBERT, M. R. The atomic weight of lead of radioactive origin. *J. Am. Chem. Soc.*, 34: 1329, 1914.

ROBINSON, G. A. History, physics and biological effects of radium. *New York State J. Med.*, 26: 96, 1926.

ROLLESTON, H. Acute constitutional symptoms due to radiation. *Brit. M. J.* 1: 1, 1923.

Russ, S. Experimental studies upon the lethal doses of x-rays and radium for human and other tumors. *Brit. J. Radiol.*, 29: 275, 1924.

Russell, W. S. Physical agents in the treatment of cancer. *Internat. J. Surg.*, 28: 245, 1915.

Saltau, W. D. Summary of radium treatment at Women's Hospital, Melbourne, during last 5 years. *M. J. Australia*, 1: 403, 1927.

Schlagintweit, E., and Sielman, H. Salt solution in radiation sickness. *Klin. Wchnschr.*, 1: 2136, 1922.

Schley, W. S. Radium in surgery. *N. York M. J.*, 114: 573, 1921.

Schneider, G. H. Investigations of biologically equivalent radium and roentgen radiation, *Strahlentherapie*, 22: 460, 1926.

Schultzer, P. Internal radium emanation therapy; cause of effect on rats of continuous emanatorium treatment. *Acta radiol.*, 6: 647, 1926.

Seide, J. Elective action of ultra-violet rays and radium. *Deutsche med. Wchnschr.*, 53: 317, 1927.

Sievert, R. M. Researches on distribution of intensity in treatment by radium at a distance as practised at Radiumhemmet. *Acta radiol.*, 5: 217, 1926.

Simpson, F. E. The use of radium in deep-seated malignant diseases and in dermatology. *Illinois M. J.*, 30: 123, 1916.

Sluys, F. New apparatus for radium treatment. *Arch. d'électric. méd.*, 36: 433, 1926.

Smith, A. B. and S. M. An electric-heated radium wax-knife. *Lancet*, 1: 1135, 1927.

Spence, T. B. The use of radium in the M. E. hospital. *Long Island M. J.*, 16: 430, 1922.

Stacy, L. J. American Radium Society form for reporting radium cases. Letter of Oct. 30, 1920.

Stenstrom, W. Methods of improving the external application of radium for deep therapy. *Am. J. Roentgenol.*, 11: 176, 1924.

Stern, S. The present status of the non-operative treatment of benign and malignant growths, as seen at the clinics abroad. *Med. Rec.*, 85: 615, 1914.

Stevens, J. T. The treatment of malignant disease by means of the new higher voltage shorter wave-length roentgen rays, radium and electrothermic coagulation. *J. M. Soc. New Jersey*, 20: 415, 1923.

Stevens, R. H. The efficient dosage in deep roentgen therapy. *J. Michigan M. Soc.*, 19: 225, 1920.

Stewart, W. T. Radium as an adjunct in treatment in some conditions met by the general practitioner. *Urol. & Cutan.* Rev., 24: 186, 1920.

Stone, C. T. Radium. *Long Island M. J.*, 15: 380, 1921.

Strauss, A. The problem of radium and surgery in the treatment of cancer. *Ohio State M. J.*, 19: 85, 1923.

Sweitzer, S. E. Radium in dermatology. *Journal-Lancet*, 35: 679, 1915.

Symposium on radium therapy. *J. A. M. A.*, 69: 144, 1917.

Turner, D. Report on the radium treatment at the Royal Infirmary, Edinburgh, during the year 1914. *Brit. M. J.*, 1: 373, 1915.

Turner, D. A case of myeloma of the sternum treated by radium. *Brit. M. J.*, 2: 218, 1915.

Ullmann, H. J. The treatment of cancer. *Am. J. Roentgenol.*, 11: 256, 1924.
Ullman, J. S. Forceps for cleaning radium needles and tubes. *Am. J. Roentgenol.*, 10: 989, 1923.
Van Allen, H. W. The present status of radiotherapy. *Boston M. & S. J.*, 189: 5, 1923.
Vander Veer, E. A. Some observations on the post-operative use of radium. *New York State J. Med.*, 22: 4, 1922.
Vaughan, J. C. Notes on cases treated with radium. *Indian M. Gaz.*, 53: 333, 1918.
deVerteuil, F. L. Radium in the treatment of skin diseases. *Radium*, 1: 3, 1913.
Viol, C. H. Protection of technical assistants and of those handling large quantities of radium or radon. *Am. J. Roentgenol.*, 15: 345, 1926.
Wachtel, H. New devices for implantation and removal of radium needles. *Am. J. Roentgenol.*, 15: 76, 1926.
Wahl, H. R. Tissue changes following radium and x-ray therapy. *South. M. J.*, 18: 387, 1925.
Weil, E. P. and Lacassagne. Aplastic pernicious anemia due to radium. *Bull. et mém. Soc. méd. d. hôp. de. Par.*, 49: 535, 1925.
Werner, P. A contribution to our knowledge of the generative processes after radium and roentgen deep therapy. *München. med. Wchnschr.*, 68: 767, 1921.
Wilkins, G. C. Experiences with the use of radium. *Boston M. & S. J.*, 186: 14, 1922.

Experimental Work

Altmann, V. A modification of the earlier method of applying radium in deep therapy. *Wien. klin. Wchnschr.*, 38: 70, 1925.
Bagg, H. J. Disturbances in mammalian development produced by radium emanation. *Am. J. Anat.*, 30: 133, 1922.
Bisceglie, V. Inoculation experiments with living Koch bacilli attenuated by radium treatment. *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 49: 272, 1926.
Bissell, J. B. The intravenous injection of radium element. *Penn. M. J.*, 18: 129, 1914–15.
Bruynoghe, R. Action of radon on antibodies. *Compt. rend. soc. de. biol.*, 95: 736, 1926.
Bull, P. Disappearance of tuberculous peritonitis eight days after the use of eleven centigrams of radium. *Tubercle*, 4: 450, 1923.
Burkser, E., Brun, I., and Bronstein, K. Bioradioactivity and the occurrence of radium in plants. *Biochem. Ztschr.*, 181: 145, 1927.
Canti, R. G., and Spear, F. G. Effect of gamma irradiation on cell division in tissue culture in vitro. *Proc. Roy. Soc.*, s. B., 102: 92, 1927.
Castelnan, R., and Loisel, P. Radio-activity of waters. *Presse méd.*, 30: 399, 1922.
Charlton, C. F. The biological effect of radium. *Radiology*, 7: 137, 1926.
Child, C. M. Quantitative factors in the susceptibility of living cell to external agents. *Radiology*, 4: 21, 1925.

Cooke, W. L. A review of six months' experience with radium. *J. M. A. Georgia*, 12: 54, 1923.

Curie, P. Measurements used in radio-activity and the radium standard. *Am. J. Roentgenol.*, 9: 607, 1922.

Cutler, M. Comparison of the effects of unfiltered and filtered radon tubes buried in rabbit muscle. *Am. J. Roentgenol.*, 16: 535, 1926.

Daels, F. Experimental provocation of tumours by means of radium. *Brit. J. Radiol.*, 30: 474, 1925.

Daels, F., and Bacten, G. Different kinds of malignant tumors experimentally obtained by means of radium. *Lancet*, 2: 666, 1926.

Dean, A. L., Jr. Results of skin tests made to determine an objective dose for radium radiations. *Am. J. Roentgenol.*, 10: 654, 1923.

Dessauer, F. The cause of the action of x-rays and gamma rays of radium upon living cells. *J. Radiol.*, 4: 411, 1923.

Dodds, E. C. and Webster, J. H. D. The metabolic changes associated with x-ray and radium treatment. *Brit. J. Radiol.*, 29: 140, 1924.

Dourmashkin, R. L. A new cystoscopic forceps especially adapted for the implantation of radium emanation "seeds." *J. Urol.*, 12: 89, 1924.

Esguerra, A., Monod, O., and Richard, G. Plastic appliances for use with curietherapy. *J. de radiol. et d'électrol.*, 7: 49, 1923.

van Eweyk, C., et al. Experimental studies on the effect of radium bromide upon metabolism. *Strahlentherapie*, 19: 789, 1925.

Ewing, J. Tissue reactions to radiation. *Am. J. Roentgenol.*, 15: 93, 1926.

Failla G., and Quimby, E. H. The economics of dosimetry in radiotherapy. *Am. J. Roentgenol.*, 10: 944, 1923.

Failla, G., Quimby, E. H. and Dean, A. Some problems of radiation therapy. *Am. J. Roentgenol.*, 9: 479, 1922.

Failla, G. Ionization measurements. *Am. J. Roentgenol.*, 10: 48, 1923.

Failla, G. A brief analysis of some important factors in the biologic action of radiation. *Am. J. Roentgenol.*, 12: 454, 1924.

Failla, G., Adair, F., Quimby, E. H., Sugiura, K., Arnell, J. C., and Goldsmith, N. W. Dosage study relative to therapeutic use of unfiltered radon. *Am. J. Roentgenol.*, 15: 1, 1926.

Fernau, A. The biologic point of action of radium rays. *Strahlentherapie*, 15: 532, 1923.

Fernau, A. The action of penetrating radium rays on serum albumin and egg albumin. *Biochem. Ztschr.*, 167: 380, 1926.

Fischer, R., and Kotzareff, A. Biologic researches on the serum of cancer before and after injections of radium emanation. *Bull. Acad. de méd., Paris*, 90: 334, 1923.

Fisher, A. G. T. Experimental production of acute and chronic arthritis and articular neoplasm by radium. *Brit. M. J.*, 1: 319, 1927.

Frazier, C. N. Radium; a résumé of its physical and therapeutic properties. *China M. J.*, 38: 341, 1924.

Freund, H. Intraperitoneal use of radium. *Deutsche med. Wchnschr.*, 40: 1252, 1914.

Fuerstenberg, A. Treatment with radium emanation. *Radium*, 1: No. 1, p. 12, 1913.

Gaylord, H. R., and Stenstroem, W. K. Comparative measurements between radium and x-rays concerning energy absorbed at depth. *Am. J. Roentgenol.*, 10: 56, 1923.

Glasser, O. Newer investigations of gamma-ray dosage of radium. *J. Radiol.*, 4: 386, 1923.

Graziadei, G. Effects of radium emanations on the fermentation of lactose and glueose induced by bacillus coli. *Riforma med.*, 40: 315, 1924.

Greinacher, H. On a new direct reading measuring apparatus for ions (ionometer). Radium in *Biol. u. Heilk.*, 2: p. 137, 1912–13.

Grzywo-Dabrowski, W. The effeet of radium rays upon the central nervous system of the mouse. *Rev. Neurol.*, 29: 1126, 1922.

Hektoen, L., and Corper, H. J. Effect of injection of active deposit of radium emanation on rabbits. *J. Infect. Dis.*, 31: 305, 1922.

Heublein, A. C., and Quick, D. A preliminary report on the use of an absorbable filter with bare tubes of radium emanation. *Am. J. Roentgenol.*, 14: 116, 1925.

Hogler, F. Symptoms, pathogenesis and radium therapy of erythremia. *Wien. Arch. f. inn. Med.*, 4: 65, 1922.

Holtermann, C. Vital staining as affected by roentgen and radium rays. *Strahlentherapie*, 17: 362, 1924.

Hosokawa, T. The effect of radium bromide administered intravenously or per os as respects the fixation of radium in the body and the intermediary metabolism. *Strahlentherapie*, 19: 546, 1925.

Hudson, R. V. Skin and tumour reactions and their bearing upon radiotherapy. *Brit. J. Radiol.*, 30: 432, 1925.

Itchikawa, K. Curiegraphy of experimental tumors by intravenous injection of serum charged with emanation of radium into the rabbit. *Bull. de l' Ass. franc. p. l'étude du cancer*, Par., 14: 193, 1925.

Jonquieres, E. Tolerance of the eye to the action of radium. *Rev. Asoc. méd. argent.*, 34: 1247, 1921.

Jüngling, O., and Beigel. W. The root reaction of vicia faba equina. *Strahlentherapie*, 14: 423, 1922.

Kotzareff, A., and Mollow, M. The action of radium emanation on the uterus and ovaries of guinea-pigs. *Gynéc. et Obst.*, 6: 244, 1922.

Kotzareff, A. Absence of affinity of injected radium-emanation for cancerous tissues; comment on Ferroux and Lacassagne's article. *Compt. rend. Soc. de biol.*, 93: 1148, 1925.

Laborde, S. Dosimetry in radium therapy. *Arch. d'électric. méd.*, 30: 14, 1922.

Lacassagne, A., and Ferroux, R. Experiment demonstrating that radium emanation has no elective affinity for cancer tissue. *Compt. rend. Soc. de biol.*, 93: 1356, 1925.

Lazarus-Barlow, W. S. The selection of gamma rays or x-rays for radiotherapeutic purposes. *Arch. Radiol. & Electroth.*, 26: 355, 1922.

Lequeux, P., and Chomé, E. Bactericidal action of radium. *Arch. mens. d'obst. et de gynec.*, 8: 698, 1919.

Levin, I. Intraperitoneal insertion of buried capillary glass tubes of radium emanation. *J. A. M. A.*, 79: 2074, 1922.

LEVIN, I., and LEVINE, M. The action of buried glass capillaries of radium emanation on plant and animal tissues. *J. A. M. A.*, 83: 1645, 1924.

LEVINE, M. The effects of radium emanation on the crown gall tissue. *Am. J. Roentgenol.*, 14: 221, 1925.

LYSHOLM, E. Apparatus for the production of a narrow beam of rays in treatment by radium at a distance. *Acta Radiol.*, 2: 516, 1923–24.

MALLET. Direct determination of the gamma rays of radium by an ionomicrometer. *Bull. et mém. Soc. de radiol. méd. de France*, 11: 272, 1923.

MALLET, L. Production of luminous and ultraviolet radiation in water and organic substances by means of gamma radiation. *Compt. rend. Soc. de biol.*, 95: 661, 1926.

MALLET, L., and PSAUME. Surface radium therapy with molded appliances. *Arch. internat. de laryngol.*, [*etc.*], 30: 785, 1924.

MARSHALL, J. A. A laboratory and clinical study of the bactericidal action of solutions of radium emanation. *California State J. M.*, 20: 8, 1922.

MATTHEWS, H. B. The effects of radium rays upon the ovary. *Surg., Gynec. & Obst.*, 38: 383, 1924.

MATTHEWS, H. B. The measurement of the biological action of x-rays and gamma rays (Edit.) *Brit. M. J.*, 1: 346, 1915.

MONTGOMERY, D. W., and CULVER, G. D. Conservation of normal tissue after treatment with radium. *Am. J. Roentgenol.*, 12: 526, 1924.

MOTTRAM, J. C. Observations upon the action of radium and x-rays on the mononuclear leucocytes of the blood of rats. *Proc. Roy. Soc. Med.* (Pathol. Sect.), 15: 1, 1921–22.

MOTTRAM, J. C. Some effects of exposure to radium upon the alimentary canal. *Arch. Radiol., & Electrotb.*, 28: 28, 1923.

MOTTRAM, J. C. The skin reactions to radium exposure and their avoidance in therapy. *Brit. J. Radiol.*, 29: 174, 1924.

MOTTRAM, J. C. Reaction of the skin to a radium exposure. *Brit. J. Radiol.*, 30: 387, 1925.

MOTTRAM, J. C. Survival curves of cells under radiation. *J. Cancer Research*, 11: 130, 1927.

MORROW, H., and TAUSSIG, L. Statistics and technique in the treatment of malignant disease of the skin by radiation. *Am. J. Roentgenol.*, 10: 212, 1923.

MUIR, J. Advantages of the "loading slot" in radium emanation implantation. *J. Urol.*, 11: 319, 1924.

NEILL, W. JR. An instrument for the implantation of bare radium emanation tubes into the tissues. *Am. J. Roentgenol.*, 10: 871, 1923.

NEWCOMET, W. S. The superficial reaction of radium as a guide to dosage. *Am. J. Roentgenol.*, 9: 34, 1922.

OCHSNER, A. J. The use of roentgen rays and radium from the standpoint of the clinical surgeon. *Internat. Clin.*, s. 34, 4: 104, 1924.

PARRY, R. H. The basis in experimental pathology for radium therapy of malignant disease. *Brit. J. Radiol.*, 29: 3, 1924.

PENDERGRASS, E. P., et. al. Effect of radium on the normal tissues of the brain and spinal cord of dogs, and its therapeutic application. *Am. J. Roentgenol.*, 9: 553, 1922.

Perussia, F. Is there a carcinoma dose in radium therapy? *Radiol. méd.*, 9: 20, 1922.

Pétchenko, B. Effect of radiation on amebae. *Ann. de Roentgenol. et radiol.*, 2: 40, 1926.

Petrow, N., and Kusmina, E. Experimental and clinical experiences with introduction of radon in normal tissues and tumors. *Deutsche med. Wchnschr.*, 52: 622, 1926.

Ponzio, M. Experiments on selective properties of radium and roentgen rays. *Strahlentherapie*, 25: 708, 1927.

Proescher, F. The pathological anatomical changes in guinea pigs killed by exposure to high concentration of radium emanation. *Radium*, 1: 5; 9, 1913.

Proescher, F. The intravenous injection of soluble radium salts. *Radium*, 2: 45, 1913–14; 61, 1914.

Proescher, F. The influence of intravenous injection of soluble radium salts in high blood pressure. *Radium*, 3: 1; 17, 1914.

Proescher, F., and Almquest, B. R. Contribution on the biological and pathological action of soluble radium salts—with special reference to its therapeutic value in pernicious anemia and leukemia. *Radium*, 3: 65, 1914.

Proust, R. Penetrating radiotherapy by x-rays and radium. *Arch. Radiol. & Electroth.*, 27: 121, 1922.

Quick, D. A., and Johnson, F. M. A new type of applicator for use with radium emanation. *Am. J. Roentgenol.*, 9: 53, 1922.

Quimby, E. H. Effect of the size of radium applicators on skin doses. *Am. J. Roentgenol.*, 9: 671, 1922.

Quimby, E. H. A simple nomogram for the determination of radium skin doses. *Am. J. Roentgenol.*, 10: 574, 1923. Radio-activity measurements. *Ann. Rep. Dir. Bur. Standards*, 1918.

Redfield, A. C., and Bright, E. M. The effects of radium rays on metabolism and growth in seeds. *J. Gen. Physiol.* 4: 297, 1922.

Redfield, A. C., Forbes, A. and Redfield, E. S. The action of beta rays of radium on excitability and conduction in the nerve trunk. *Am. J. Physiol.*, 59: 203, 1922.

Redfield, A. C., and Bright, E. M. Hemolytic action of radium emanation. *Am. J. Physiol.*, 65: 312, 1923.

Redfield, A. C., and Bright, E. M. The physiological action of ionizing radiations. *Am. J. Physiol.*, 68: 62, 1924.

Regaud, C. Some biologic aspects of the radiation therapy of cancer. *Am. J. Roentgenol.*, 12: 97, 1924.

Reinhard, M. C., and Buchwald, K. W. Influence of intense x-ray and gamma ray radiation on cholesterol. *J. Biol. Chem.*, 73: 383, 1927.

Reitter, G. S., and Martland, H. S. Leucopenic anemia of the regenerative type due to exposure to radium and mesothorium. *Am. J. Roentgenol.*, 16: 161, 1926.

Richards, A. Recent studies on the biological effects of radio-activity. *Science*, N. S., 42: 287, 1915.

Rocchi, G. Radium therapy. Beta therapy. Effect of a magnetic field in the direction of beta radiation. *Radiol. med.*, 12: 762, 1925.

ROSENBLOOM, J. A study of the urinary nitrogen and sulphur partition in a case of rheumatoid arthritis treated with intravenous injections of radium salts. *Am. J. M. Sc.*, 149: 718, 1915.

ROSENBLOOM, J. A study of the effects of radium on metabolism. *J. Metab. Research*, 4: 75, 1923.

ROSSELET, A. Radioimmunization. *Schweiz. med. wchnschr.*, 56: 670, 1926.

ROTH, S. C., and MORTON, J. J. The immediate effect of radium and x-rays on enzyme action. *Am. J. Roentgenol.*, 10: 407, 1923.

RUD, E. Blood examination of the staff of roentgenologic and radium institutions. *Ugeskr. f. Laeger*, 86: 438, 1924.

RUSS, S., and SCOTT, G. M. Growth of tumor in tissues, exposed to x-rays and radium. *Lancet*, 1: 815, 1927.

RUTHERFORD, E. Artificial disintegration of the elements. *Nature*, 109: 584, 109: 614, 1922.

SEIL, H. A., VIOL, C. H., and GORDON, M. A. The elimination of soluble radium salts taken intravenously and per os. *N. York M. J.* (etc.), 101: 896, 1915.

SIEVERT, R. M. The intensity distribution of gamma rays near medicinal radium preparations. *Acta Radiol.*, 2: 70, 1923.

SIEVERT, R. M. Secondary rays in radium therapeutics. *Acta Radiol.*, 2: 268, 1923.

SITTENFIELD, M. J. Experimental studies on the biological effects of radium upon tissues growing in vitro. *Am. J. Roentgenol.*, 15: 155, 1926.

SPURLING, R. G., and LAWRENCE, J. S. The direct effect of radium irradiation on leukocytes. *Am. J. M. Sc.*, 169: 157, 1925.

STENSTROM, W. Consideration of body dose in radiation therapy. *J. Cancer Research*, 8: 30, 1924.

SUGIURA, K., and FAILLA, G. Some effects of radium radiations on white mice. *J. Gen. Physiol.*, 4: 423, 1922.

TURNER, D. The dosage of radium. *Brit. M. J.*, 1: 100, 1923.

VIOL, C. H. Radium and its rays. *Radium*, 1: No. 1, p. 4, 1913.

VIOL, C. H. The production and decay of radioactive matter. *Radium*, 1: No. 2, p. 3, 1913.

VIOL, C. H. A comparison of radiation dosages attainable by use of radium on and within tumors. *Am. J. Roentgenol.*, 9: 56, 1922.

WAHL, H. R. Cellular reactions following x-ray and radium therapy. *J. Missouri M. A.*, 21: 173, 1924.

WEIL, R. The treatment of parotid tumors by radium. *J. Cancer Research*, 1: 121, 1916.

WEIS, H. A. A contribution to the study of the effects of radium upon rabbit ovaries. *Surg. Gynec. & Obst.*, 36: 373, 1923.

WESTMAN, A. The influence of the roentgen and radium rays on phagocytosis. *Acta Radiol.*, 2: 57, 1923.

WHITTEMORE, C. F. An apparatus for the purification of radium emanation. *J. Radiol.*, 3: 384, 1922.

WINKLER, F. On the effects of radium emanation. *Wien. med. Wchnschr.* 62: 2683, 1912.

WOOD, F. C., and PRIME, F. JR. The action of radium on transplanted tumors of animals. *Ann. Surg.*, 62: 751, 1915.

Wood, F. C., and Prime, F., Jr. The action of radium on transplanted animal tumors. *Strahlentherapie*, 12: 1071, 1921.

Zander, R. Radium dosage. *Arch. f. Gynäk.*, 115: 253, 1921.

Zunz, E., and LaBarre, J. Effects of gamma rays on coagulation of blood, glycemia and calcemia. *Ann. de physiol.*, 3: 844, 1927.

Zwaardemaker, H. Method of investigating effect of radio-active substance upon heart. In Abderhalden, E. Handb. d. biol. Arbeitsmeth., Abt. 5, Teil 4, pt. 2, pp. 1715, 1927.

Zwaardemaker, H., and Zeehuisen, H. Radium dosage and frequency of heart beat. *Arch. f. d. ges. Physiol.*, 217: 469, 1927.

Surgery

Abbé, R. The efficiency of radium in surgery. *Ohio State M. J.*, 10: 461, 1914.

Bissell, J. B. The surgical status of radium treatment of cancer. *Internat. J. Surg.*, 27: 324, 1914.

Blair, V. P. Repair of defects caused by surgery and radium in cancer of hand, mouth and cheek. *Am. J. Roentgenol.*, 17: 99, 1927.

Boggs, R. H. Treatment of glandular metastases of carcinoma. *Am. J. Roentgenol.*, 9: 117, 1922.

Burnam, C. F. New growths of the mediastinum; with special reference to their treatment with radium. *J. A. M. A.* 69: 989, 1917.

Chase, W. B. Radium in non-malignant conditions. *Long Island M. J.*, 9: 241, 1915.

Clark, W. L. New conceptions relative to the treatment of malignant disease with special reference to radium in needles. *Penn. M. J.*, 24: 214, 1921.

Cushway, B. C. Practical application of radiation therapy in conjunction with surgery. *Illinois M. J.*, 48: 264, 1925.

Dean, A. L. The treatment of teratoid tumors of the testis with radium and the roentgen ray. *J. Urol.*, 13: 149, 1925.

Desjardins, A. U. The reaction of abdominal tumors to radiation. *J. A. M. A.*, 83: 109, 1924.

Durham, P. E. Surgical exposure of deep-seated inaccessible neoplasms for proper implantation with radium emanation in capillary glass tubes by basal route. *New York State J. Med.*, 26: 301, 1926.

Figi, F. A. Bare radium tubes in treatment of tumors around the head and neck. *Minnesota Med.*, 9: 13, 1926.

Finzi, N. S. The use of radium in combination with x-rays and surgery. *Brit. J. Radiol.*, 30: 430, 1925.

Harris, W. L. Closure of bronchial fistula of 12 years' standing by use of radium. *Med. J. & Rec.* 120: 590, 1924.

Harrison, F. C. The use of radium in postoperative conditions. *Internat. J. Surg.*, 30: 98, 1917.

Herbst, R. H. *J. A. M. A.*, 72: 1610, 1919. *Surg., Gynec. & Obst.*, 29: 311, 1919.

Holding, A. F. The treatment of cancer by electrical methods; with and without surgery and radium. *N. York, M. J.*, 100: 557, 1914.

Kennedy, W. H. Radium applicator for treatment of lesions about head, face and neck. *J. A. M. A.*, 86: 1907, 1926.

KNAPP, A. Orbital changes produced by radium in cancer of the upper jaw. *J. A. M. A.*, 81: 1849, 1923.

KOTZAREFF, A. Internal radon therapy in cancer; danger of intravenous injections. *Néoplasmes*, 6: 348, 1927.

LECLERC, C. The association of surgery and radium in cancer and particularly in cancer of the uterus. *Bull. et. mém. Soc. de chir. de Paris*, 48: 666, 1922. *Presse méd.*, 30: 731, 1922.

LEVIN, I. The relation between the surgical treatment and radiotherapy of cancer. *Med. Rec.*, 86: 615, 1914.

LEVIN, I. The local application of radium in surgery. *Penn. M. J.*, 18: 121, 1914–15.

LEVIN, I. Comparative action of electrothermic coagulation; intratumoral insertion of glass capillaries of radium emanation on malignant tumors. *Tr. Sect. Path. & Physiol., A. M. A.*, p. 94, 1925.

LEVIN, I. Radon therapy in cancer of abdomen and pelvic cavities; intraperitoneal insertion of capillary tubes of radon. *J. A. M. A.*, 90: 273, 1928.

MARTIN, C. L., and ROGERS, F. T. The effect of irradiation on the ureter. *Am. J. Roentgenol.*, 16: 215, 1926.

MAYO, W. J. The relative values of surgery and radiotherapy. *Minnesota Med.*, 8: 7, 1925.

MORRISON, L. B. X-ray and radium treatment of non-malignant diseases of the uterus. *Boston M. & S. J.*, 191: 13, 1924.

PANCOAST, H. K. Modern treatment of cancer of lip. *Surg., Gynec. & Obst.*, 34: 589, 1922.

PINCH, A. E. H. Leukoplakia of the cheeks. Report of the Work at the Radium Institute, London, Jan. 1 to Dec. 31, 1922. *Radium*, 2: 46, 1923.

RANSON, J. R. Radiation methods in the treatment of malignancies. *J. Radiol.*, 6: 257, 1925.

REITTER, G. S. The radiation treatment of non-malignant conditions. *J. M. Soc. New Jersey*, 23: 489, 1926.

SCHWYZER, A. Radium; its therapeutic uses in surgery. *Minnesota Med.*, 4: 533, 1921.

SMITH, A. B. and S. M. Operative radium-needle stand. *Lancet*, 2: 605, 1926.

STEVENSON, W. C. The effects of radium treatment on war injuries in the neighborhood of nerves. *Brit. M. J.*, 1: 862, 1920.

TYLER, A. F. Carcinoma of lingual thyroid with metastases in the lungs. *J. Radiol.*, 4: 381, 1923.

VOLTZ, F. The exclusive treatment of carcinoma of the cervix by radiation. *Klin. Wchnschr.*, 4: 1396, 1925.

WOLF, W. A new method for the stimulation of endocrine glands with radium. *Am. J. Roentgenol.*, 15: 520, 1926.

GYNECOLOGY

AMREICH, I. Radium in gynecology. *Wien. klin. Wchnschr.*, 40: (supp. 42), 4, 1927.

BARROW, S. C. Radiation treatment of non-malignant diseases of the female pelvis. *New Orleans M. & S. J.*, 80: 231, 1927.

Belgrano, C. R. Radium therapy in cancer of female genital organs. Ten cases. *Actinoterapia*, 7: 63, 1928.

Block, F. B. Radium in gynecology. *Arch. Physical Therapy*, 7: 137, 1926.

del Buono, P. Irradiation of pituitary gland in treatment of gynecological disorders. *Clin. ostet.*, 29: 181, 1927.

Crile, G. W. Surgery versus roentgen ray and radium therapy in the treatment of tumors of the uterus. *J. Iowa M. Soc.*, 15: 1, 1925.

Danforth, W. C. The use of radium in gynecology. *Illinois M. J.*, 49: 80, 1926.

Dautwitz, F. External irradiation with radio-active substances in gynecology. *Fortschr. a. d. Geb. d. Röntgenstrahlen* (Kongress-hft.), 36: 58, 1927.

Dean, A. L., Jr. Ulceration of urinary bladder as late effect of radium applications to uterus. *J. A. M. A.*, 89: 1121, 1927.

Eymer, H. Radium in gynecology. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, (Kongress hft.), 36: 60, 1927; *Strahlentherapie*, 26: 65, 1927.

Eymer, H. Radium in gynecology. *Deutsche med. Wchnschr.*, 53: 2069, 1927.

Faerber, H. False cyst of uterus resulting from radium and roentgen irradiation of inoperable cancer of portio. *Monatschr. f. Geburtsh. u. Gynäk.*, 79: 45, 1928.

Gendreau, J. E. Infectious complications of radiotherapy of cervix uteri. *Am. J. Phys. Therapy*, 5: 57, 1928.

Handorn. Case of incrusted ulcer of urinary bladder as late result of radiation therapy. *Zentralbl. f. Gynäk.*, 52: 507, 1928.

Heidler, H. Gangrenous dissecting cystitis due to radium (Stockel, 1902). *Ztschr. f. Geburtsh. u. Gynäk.*, 92: 1, 1927.

Jones, T. E. The role of radium in benign and malignant tumors of the uterus. *Illinois M. J.*, 45: 255, 1924. *Wisconsin M. J.*, 22: 466, 1924.

Kahn, I. W. Ulceration of bladder simulating carcinoma following the use of radium in cervix. *Urol. & Cutan. Rev.*, 31: 360, 1927.

Kaplan, I. I. New type of applicator for use in treatment of malignancy of cervix. *Am. J. Roentgenol.*, 17: 360, 1927.

Kaplan, I. I. Radiation treatment of malignancy of cervix by radium emanation. *Radiology*, 9: 314, 1927.

Keene, F. E. Radium in gynecology. *Atlantic M. J.*, 31: 50, 1927.

Koenig, M. Radium therapy in hemorrhagic metritis. *Gynéc. et Obst.*, 4: 317, 1921.

Martius, H. So-called stimulating irradiation in gynecology. *Strahlentherapie*, 21: 242, 1926.

Matthews, H. B. The effects of radium rays upon the ovary. *Am. J. Obst. & Gynec.*, 6: 614, 1923.

Meigs, J. V. Radium therapy in gynecology. *New England J. Med.*, 199: 258, 1928.

Miller, C. J. Contraindications to the use of radium in gynecology. *Internat. Clin.*, 1: 120, 1926.

Muir, J. Radium emanation treatment of cervical cancer. *Med. J. & Rec.*, 125: 806, 1927; 126: 243; 291; 422; 502; 551, 1927.

Muir, J. Radon therapy in benign lesions of uterus. *Arch. Physical Therapy*, 8: 587, 1927.

Muir, J. Radon therapy of cervical cancer; treatment of advanced lesions and recurrence after surgery. *Med. J. & Rec.*, 126: 725, 1927.

Muir, J. Radon therapy of cervical cancer; technical details of application. *Med. J. & Rec.*, 127: 472, 1928.

Norris, C. C. Radium in gynecology. *J. A. M. A.*, 90: 199, 1928.

Norris, C. C., and Vogt, M. E. Radiation in gynecology. *S. Clin. N. Amer.*, 7: 315, 1927.

Portmann, U. V. The general role of roentgen rays in the treatment of benign and malignant tumors of the uterus. *J. Iowa M. Soc.*, 15: 3, 1925.

Richards, G. E. Radiation in the treatment of benign diseases of the female pelvis. *Canad. M. A. J.*, 15: 382, 1925.

Seeligmann, G. Two years' experience with the combination treatment of surgery and radium rays in cases of carcinoma uteri. *Am. J. Obst. & Gynec.*, 9: 66, 1925.

Seitz, L. Stimulating irradiation in diseases of women. *Strahlentherapie*, 24: 227, 1926.

Sellheim, H. Do women with hemorrhages recover better after hysterectomy or after irradiation? *Münch. med. Wchnschr.*, 70: 1406, 1923.

von Seuffert, E. R. Radium treatment of benign affections. *Strahlentherapie*, 27: 81, 1927.

Simpson, F. E., and Flesher, R. E. New uterine screen and introducer for inserting radon tubes into uterus. *J. A. M. A.*, 86: 1005, 1926.

Smith, W. S. Report of 257 gynecological cases treated with radium alone or combined with surgery. *S. Clin. N. Amer.*, 7: 1083, 1927.

Solomon, I., and Gibert, P. Menopause after irradiation of uterus. *Arch. d'électric. méd.*, 36: 503, 1926.

Stacy, L. J. The treatment of benign conditions of the pelvis with radium. *Am. J. Roentgenol.*, 9: 658, 1922.

Stevens, T. G. Radium in gynecology. *Clin. J.*, 56: 421, 1927.

Van de Velde, T. H. Radiotherapy in adnexitis. *Zentralbl. f. Gynäk.*, 44: 994, 1920.

Vignes, H. & Cornil, L. Dystocia due to cicatricial stenosis of the cervix consecutive to an intracervical application of radium. *Bull. Soc. d'obst. et de gynéc. de Paris*, 12: 190, 1923. *Progrés méd.*, 36: 315, 1923.

Wallon, E. Measures for combating infectious complications of radium therapy of uterine cancer. *Presse méd.*, 36: 1061, 1928.

Watkins, T. J. Report of three cases of abdominal section for uterine fibroids after the use of radium. *Surg., Gynec. & Obst.*, 36: 433, 1923.

Weigand, H. Radium in gynecology. *Fortschr. a. d. Geb. d. Röntgenstrahlen* (Kongresshft.), 36: 64, 1927.

Weigand, H. Technic of radium application in gynecology. *Strahlentherapie*, 27: 54, 1927.

Werner, P. Irradiation of spleen or pituitary as substitute for irradiation of ovary in young women. *Wien. klin. Wchnschr.*, 40: 197, 1927.

Eye

Corbett, J. J. The effect of radium on glaucoma. *Boston M. & S. J.*, 190: 1124, 1924.

Flemming. Experimental and clinical studies on the action of radio-active rays in eye diseases. *Arch. f. Ophth.*, 84: 345, 1913.

Lane, L. A. Radium in ophthalmology with special reference to its use in benign affections. *J. A. M. A.*, 83: 1838, 1924.

Meesmann, A. Cataract due to radium and roentgen rays. *Klin. Monatsbl. f. Augenh.*, 81: 259, 1928.

Pomeroy, L. A., and Strauss, A. Radium in diseases of eye, ear, nose and throat. *Laryngoscope*, 36: 437, 1926.

Stock, W. Radiotherapy in ophthalmology. *Med. Klin.*, 22: 1834, 1926.

Withers, S. Value of radiation therapy in ophthalmology. *Am. J. Ophth.*, 7: 514, 1924.

Skin

Aikins, W. H. B. Radium and trichloracetic acid in dermatology. *Canad. Pract. & Rev.*, 40: 479, 1915.

Aikins, W. H. B., and Harrison, F. C. A case of naevus linearis treated by radium. *Urol. & Cutan. Rev.*, 27: 212, 1923.

Barcat, J. Radium in dermatology. *Paris méd.*, 12: 106, 1922.

Balot, M. J. Radio-resistance of cutaneous epitheliomas previously irradiated. *J. de radiol. et d'électrol.* 12: 91, 1928.

Broeman, C. J. Radium in dermatology. *Ohio State M. J.*, 17: 841, 1921.

Bryant, F. Report of 146 cases of skin affections treated with radium. *Boston M. & S. J.*, 188: 803, 1923.

Burns, F. S. Radium in the treatment of non-malignant diseases of the skin. *Boston M. & S. J.*, 191: 16, 1924.

Carter, L. J. The newer methods of treating skin diseases. *Canad. M. A. J.*, 15: 148, 1925.

Crocket, R. H. Radiation problems in dermatology. *Texas State J. Med.*, 22: 458, 1926.

Degrais, P., and Bellot, A. Radium therapy of epitheliomas. *Clinique*, Paris, 22: 397, 1927.

Eller, J. J. Radiotherapy in dermatology; x-rays, radium, endotherapy and other physical agents in dermatology. *Med. J. & Rec.*, 125: 541; 593, 1927.

Holding, A. F. The relative value of radium in dermatology. *J. A. M. A.*, 63: 741, 1914.

Kumer, L. Radium therapy in skin diseases. *Wien. klin. Wchnschr.*, 41: 444, 1928.

Lomholt, S. The effects of the alpha rays on the skin and their value in the treatment of some dermatoses *Acta dermato.*, Helsingfors, 3: 463, 1922.

Mackay, H. Radium in dermatology. *Canad. M. A. J.*, 16: 1352, 1926.

Marquis, E. Extreme radio-resistance of epitheliomas previously irradiated. *Bull. de l'Assoc. franç. p. l'étude du cancer*, 17: 53, 1928.

McCullough, J. F. Radium therapy in skin diseases. *Urol. & Cutan. Rev.*, 31: 32, 1927.

McHutchison, J. P., and Brown, W. H. New development in radium therapy; application of later disintegration products of radium to treatment of certain skin conditions. *Lancet*, 1: 755, 1926.

Möbius, H. Ten years' radium treatment in skin diseases. *Med. Klin.*, 21: 967, 1925.

Pusey, W. A. Radium in cutaneous lesions. *Penn. M. J.*, 18: 134, 1914–15.

Reyn, A. Value of concentrated arc light treatment in cases of roentgen and radium lesions of skin. *Radiology*, 6: 457, 1926.

Robinson, G. A. Radium therapy in dermatology. *Am. J. Roentgenol.*, 14: 130, 1925.

Roussy, G., and Laborde, S. Radio-resistance of skin cancer previously irradiated. *Bull. de l'Assoc. franç. p. l'étude du cancer*, 16: 180, 1927.

Ryerson, G. S. Radium in epithelioma and allied affections. *Canad. J. Med., & Surg.* 35: 264, 1914.

Saalfeld, E. Headache and menstrual disturbance following the use of radium in dermatology. *Dermat. Ztschr.*, 54: 533, 1928.

Simpson, A. C. The relative value of radium and x-ray in treatment of skin diseases and cancer. *South. M. J.* 7: 815, 1914.

Simpson, F. E. Radium in skin diseases. *J. A. M. A.*, 61: 80, 1913.

Simpson, F. E. Radium. Its use and limitations in skin diseases. *J. A. M. A.*, 63: 737, 1914.

Simpson, F. E. Radium in the treatment of cancer and various other diseases of the skin. *J. A. M. A.*, 67: 1508, 1916.

Taussig, L. R. The limitations of radium therapy in dermatology. *Am. J. Roentgenol.*, 14: 121, 1925.

Miscellaneous

Aikins, W. H. B. Radium therapy. *Canad. M. A. J.*, 12: 736, 1922.

Aikins, W. H. B. Radium and surgery. *Internat. J. Surg.*, 36: 189, 1923.

Anderson, W. S. Further studies in the use of radium in cancer. *J. Tennessee M. A.*, 15: 193, 1922.

Angle, E. J. and Owen, L. J. A report on radium therapy. *Nebraska M. J.*, 8: 236, 1923.

Apert, E. Hereditary contraction of palmar fascia; efficiency of radium emanation. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 49: 1502, 1925.

Ayres, W. Report of two cases of tumor of the kidney treated by radium. *Internat. J. Surg.*, 35: 124, 1922.

Bachem, A. Radium and roentgen rays as different agents in superficial and deep therapy. *Am. J. Roentgenol.*, 11: 13, 1924.

Bissell, J. B. The medicolegal aspects of radium therapy. *Med. Rec.*, 92: 102, 1917.

Boggs, R. H. Radium and mesothorium in conjunction with roentgen therapy. *Am. J. Roentgenol.*, 2: 731, 1914–15.

Boggs, R. H. The value of radium in the treatment of cancer. *N. York M. J.*, 109: 488, 1919.

Boltwood, B. B. The life of radium. *Science*, n.s., 42: 851, 1915.

Bordier, H. Cancer of radiologists. *Arch. d'électric. méd.*, 36: 500, 1926.

Bovie, W. T. The physiological action of radiation. *J. Med. Research*, 39: 271, 1918.

Bowing, H. H. Radium and roentgen ray treatment in metastatic testicular tumors. *J. Radiol.*, 3: 519, 1922.

Broeman, C. J. Radium in medicine. *Ohio State M. J.*, 20: 226, 1924.

Broeman, C. J. Indications and contra-indications for radium. *W. Virginia M. J.*, 22: 460, 1926.

Bugbee, H. G. Some recent advances in urological surgery. *N. York M. J.* 116: 489, 1922.

Burrows, A. A report of the Work of the Manchester and District Radium Institute (Manchester, England).

Burrows, A. The problem of the radium therapy of cancer. *Brit. M. J.*, 2: 33, 1922.

Cameron, W. H. Radium in the treatment of cancer. *Radium*, 4: 37, 1914.

Cameron, W. H. Radium in military surgery. *Penn. M. J.*, 19: 449, 1916.

Cameron, W. H. Radium in war surgery. *Penn. M. J.*, 21: 579, 1918.

Cameron, W. H. Radium in French military surgery. *Penn. M. J.*, 19: 906, 1915–16.

Cameron, W. H. The treatment of alveolar pyorrhea with radium emanation. *Radium*, 2: 41, 1913.

Chase, C. Remarks on the dosage of radium and the form and method of its application. *Urol. & Cutan. Rev.*, 26: 14, 1922.

Chase, C. Two important points from the radium therapeutist's standpoint regarding cancer immunity. *Am. J. Roentgenol.* n. s., 10: 167, 1923.

Clark, W. L. The rôle of radium needles in the treatment of neoplastic disease. *Am. J. Roentgenol.*, 10: 204, 1923.

Clark, W. L. The treatment of neoplastic diseases by combined methods. *J. Indiana M. A.*, 17: 271, 1924.

Clark, W. L., Morgan, J. D., and Asnis, E. J. Objections to the use of radium emanation in bare tubes. *Am. J. Roentgenol.*, 12: 519, 1924.

Collins, C. D. The present status of radium as a curative agent. *J. Ophth. Otol. & Laryngol.*, 28: 426, 1924.

Crain, R. C. Some factors in radium treatment. *Illinois M. J.*, 47: 110, 1925.

Crockett, R. H. Reradiation. *Texas State J. Med.*, 24: 439, 1928.

Cullen, T. S. America's place in the surgery of the world. *Surg., Gynec. & Obst.* 25: 376, 1917.

Cutler, M. Comparison of effects of unfiltered and filtered radon tubes buried in rabbit muscle. *Am. J. Roentgenol.*, 16: 535, 1926.

Daels, F. et al. Radium therapeutic drainage of the true pelvis. *Gynéc. et Obst.*, 4: 459, 1921.

Daland, E. M. Radium therapy—use and abuse. *New England J. Med.*, 198: 1005, 1928.

Derby, G. S. X-ray and radium in the non-malignant diseases of the eye. *Boston M. & S. J.*, 191: 20, 1924.

Desjardins, A. U. Protection against radiation. *Radiology*, 1: 221, 1923.

Desjardins, A. U. The present status of radiation therapy in cancer. *Journal-Lancet*, 44: 103, 1924.

Dieulafé, L. The campaign against cancer. *Paris méd.*, 12: 41, 1922.

Dobrovolskaïa-Zavadskaïa. Modifications of striated muscle produced by prolonged exposures to radium introduced locally. *J. de radiol. et d'électrol.*, 8: 49, 1924.

Doub, H. P. Radiation reactions and their treatment. *Ann. Clin. Med.*, 5: 715, 1927.

Duane, W., and Greenough, R. B. Report of results of radium treatment at the Collis P. Huntington Memorial Hospital by the Cancer Commission of Harvard University. *Boston M. & S. J.*, 177: 359, 1917.

Duncan, R. The development of a radium and oncologic institution in California. *Mod. Hosp.*, 18: 325, 1922.

Edwards, D. J., and Bagg, H. J. Lesions of the corpus striatum by radium emanation and the accompanying structural and functional changes. *Am. J. Physiol.*, 65: 162, 1923.

Fernau, A. Action of penetrating radium rays on pseudoglobulin. *Biochem. Ztschr.* 189: 172, 1927.

Finzi, N. S. Therapy by gamma rays. *St. Barth. Hosp. Rep.*, 60: 73, 1927.

Fischer, R., and Wohlers, H. Radon therapy in grave sepsis. *Bull. Acad. de méd., Paris*, 97: 596, 1927.

Flinn, F. B. Antral Sinusitis complicated by radium poisoning. *Laryngoscope*, 37: 341, 1927.

Gherardi, B. Thoracic neoplasms. *Actinoterapia*, 4: 257, 1924.

Glasser, O. A. Distribution of the intensity of the gamma rays of radio-active substances within an absorbing medium. *Acta radiol*, 1: 475, 1921-22.

Grier, G. W. Radium therapy in surface applications. *Radiology*, 11: 474, 1928.

Guarina, C. Peculiar effect of radium on testicles. *Riforma med.*, 40: 774, 1924.

Gudzent, F. Radium emanation therapy. *Klin. Wchnschr.*, 1: 1658, 1922.

Gunsett, A., and Sichel, D. Two years of deep roentgenotherapy in the treatment of cancer. *Arch. d'électric. méd. etc.*, 34: 37, 1924.

Guttman, J. Radium in rhinoscleroma. *N. York M. J.*, 102: 711, 1915.

Guy, W. H., and Jacob, F. M. The erythema dose of radium. *Arch. Dermat. & Syphilol.*, 9: 73, 1924.

Hanford, C. W. Radium: its uses in the treatment of cancer. *Cincinnati J. Med.*, 4: 391, 1923.

Hanford, C. W. Radium therapy—uses and misuses. *Illinois M. J.*, 54: 50, 1928.

Heiner, M. Radium treatment of malignant tumors. *Strahlentherapie*, 15: 522, 1923.

Hussey, R. G., and Thompson, W. R. Radio-active radiations on enzymes. *J. Gen. Physiol.*, 9: 211, 1925.

Jentzer, A. Curietherapy and radio-active injections. *J. de radiol. et d'électrol.*, 6: 222, 1922.

Kelly, H. A. Some radium achievements. *Am. J. Surg.*, 30: 73, 1916.

Kelly, H. A. The care of radium in the hospital. *Mod. Hosp.*, 18: 406, 1922.

Knox, R. Some aspects of the cancer problem. *Am. J. Roentgenol.*, 11: 1, 1924.

Kondratjew, N. S. The effect of radium rays on oxidation mechanism in the cell. *Strahlentherapie*, 20: 771, 1925.

Kotchnéva, N. P. Effects of radon on amount of sugar in blood. *Ann. de roentgenol. et radiol.* 2: 379, 1927.

Kotzareff, A. Changes of blood and serum after local and intravenous application of radium emanation in cancer. *Schweiz. med. Wchnschr.*, 56: 151, 1926.

Krusch, P. Radium deposits. *Strahlentherapie*, 16: 575, 1923–24.

Lacassagne, A. Present conceptions of histologic processes of regression in neoplasms treated by x-rays and gamma rays. *Paris méd.*, 12: 143, 1922.

Lacassagne, A., and Gricouroff, G. Effects of radon on blood leukocytes studied by means of culture method. *J. de radiol. et d'électrol.*, 11: 573, 1927.

Lacassagne, A., and Paulin, A. Destruction of bacteriolytic principle by corpuscular rays of radon. *Compt. rend. Soc. de biol.*, 93: 1502, 1925.

Lain, E. S. The present status of radium therapy. *South. M. J.*, 15: 495, 1922.

Lawrence, H. Radium therapy. *M. J. Australia*, 1: 463, 1923.

Lawrence, W. S. On the reasons for choice—radium or x-ray, when radiotherapy is indicated. *Urol. & Cutan. Rev.*, 28: 294, 1924.

Leist, M. Effects of x-rays and radium on jaws and teeth. *Strahlentherapie*, 24: 268, 1926.

Lomholt, S. On the employment of radio-active matter in solution. *Acta Radiol.*, 2: 437, 1923–24.

Lüscher, E. Radium treatment of malignant tumors in otolaryngology. *Schweiz. med. Wchnschr.*, 56: 55, 1926.

Margreth, G. Blood cholesterol following irradiation of suprarenal gland. *Boll. d. Soc. ital. di biol. sper.*, 1: 724, 1926.

Margreth, G., and Lambranzi, M. Behavior of blood cholesterol following irradiation of liver. *Boll. d. Soc. ital. di biol. sper.*, 2: 507, 1927.

Martland, H. S., Conlon, P., and Knef, J. P. Some unrecognized dangers in the use and handling of radioactive substances. *J. A. M. A.*, 85: 1769, 1925.

Matthews, H. B., and Mazzola, V. P. Biochemical changes in blood following radium therapy; 100 irradiated cases. *Am. J. Obst. & Gynec.*, 16: 97, 1928.

Matusovszky, A. A case of six days' anuria as a result of radium irradiation. *Monatschr. f. Geburtsh. u. Gynäk.*, 65: 299, 1924.

Mayer, C. Roentgen rays and radium in research on poisonings. *Compt. rend. Soc. de biol.*, 94: 1208, 1926.

Mazérés, G. Radium therapy. *J. de radiol. et d'électrol.*, 8: 102, 1924.

Menees, T. O. Intragastric radium application. *Am. J. Roentgenol.*, 11: 561, 1924

von Mikulicz-Radecki, F. Radiotherapy of malignant tumors. *Beihefte z. Med. Klin.*, 23: 161, 1927; *Strahlentherapie*, 26: 252, 1927.

Moriarta, D. C. Radium, a recognition of its efficiency and a plea for more thorough investigation. *Med. Rec.*, 89: 410, 1916.

Moriarta, D. C. Radium—a palliative. *Am. J. Obst.*, 75: 21, 1917.

Müller, E. Lowering of blood pressure by radium baths and radium emanation. *Klin. Wchnschr.* 4: 2477, 1925.

Muir, J. Radio-activity. *Radiology*, 4: 101, 1925.

de Nabias. Three cases of cancer treated by radium therapy. *Bull. et Mém. Soc. de Chir. de Paris*, 49: 910, 1923.

NEMENOV, M., and GROSMAN, F. Radon therapy of malignant tumors. *Vestnik Roentgen. i. Radiol.*, 5: 93, 1927.

NEWCOMET, W. S., and SMOCZYNSKI, M. E. The use of radium as a therapeutic agent in the Jefferson Medical College Hospital, Philadelphia. *Therap. Gaz.* [etc.], N. S., 40: 235, 1924.

NEWELL, E. T. A consideration of the relative values of radium. *Internat. J. Surg.*, 36: 192, 1923.

NOGIER, T. Powerful reinforcement of the action of radium and x-rays in the treatment of tumors. *J. de radiol. et d'électrol.*, 7: 551, 1923.

VON NOORDEN, C., and CAAN, A. Radium treatment of hemorrhoids. *Therap. Monatsh.*, 29: 315, 1925.

OPITZ, E. Biologic phenomena during irradiation of carcinomas and their utilization for therapeutic purposes. *Monatschr. f. Geburtsh. u. Gynäk.*, 61: 232, 1923.

OPITZ, E. On the radiation biology of carcinoma. *Brit. J. Radiol.*, 30: 252, 1925.

PANCOAST, H. K., and SAWYER, W. A. The results of the use of radium for two years at the University Hospital. *Penn. M. J.*, 19: 800, 1916.

PFAHLER, G. E. Effects of x-rays and radium on the blood and general health of radiologists. *Am. J. Roentgenol.*, 9: 647, 1922.

PFAHLER, G. E. Treatment of malignant disease by radium. *Internat. J. Surg.*, 35: 423, 1922.

POWELL, W. C. Some remarks on radium. *Internat. J. Surg.*, 35: 15, 1922.

QUICK, D. Radon therapy in adequate dosage in treatment of cancer. *J. A. M. A.*, 89: 2035, 1927.

Radium treatment at the Royal Infirmary, Edinburgh. *Lancet*, 192: 546, 1917.

RAVENEL, L. J. Radiation. *J. South Carolina M. A.*, 19: 432, 1923.

REDFIELD, A. C., BRIGHT, E. M., and WERTHEIMER, J. The physiological action of ionizing radiations. *Am. J. Physiol.*, 68: 368, 1924.

REINHARD, M. C. Study of influence of radiation on cholesterol in vitro. *J. Cancer Research*, 11: 95, 1927.

RENFER, E. Myocardial necrosis following radium therapy. *Cancer*, Bruxelles, 4: 431, 1927.

RISSE. Some blood changes during roentgen and radium action. *Arch. f. Gynäk.*, 120: 181, 1923.

ROCCHI, G. Deep radiotherapy. *Policlinico* (*Surg. Sect.*) 29: 183, 1922.

ROSSELET, A. Radio-immunization. *Brit. J. Radiol.*, 32: 316, 1927.

RULISON, R. H., and MCLEAN, S. Treatment of vascular nevi with radium. *Am. J. Dis. Child.*, 25: 359, 1923.

RUSS, S., and SOMERSET, MRS. R. H. Hospital radium service. *Brit. J. Radiol.*, 31: 218, 1926.

SCHINDLER, O. Radium and mesothorium in the treatment of malignant tumors. *Radium*, 2: 1, 1913.

SCHLUNDT, H. Glossary of terms in radio-activity. *Radium*, 3: 33, 1914.

SCHMITZ, H. Uterine hemorrhages with special reference to actinotherapy. *Surg., Gynec. & Obst.*, 22: 719, 1916.

SIMPSON, F. E. Radium therapy. (Book Review) *Radium*, 1: 201, 1922.

SIMPSON, F. E. Recent developments in radium therapy. *Illinois M. J.*, 44: 327, 1923.

Sittenfield, M. J. The evaluation of x-ray and radium therapy in cancer and its future outlook. *Radiology*, 2: 74, 1924.

Sluys. Treatment by external application of radium needles. *J. de radiol. et d'électrol.*, 7: 547, 1923.

Soiland, A. Protection to the operator from unnecessary radium radiation. *Am. J. Roentgenol.*, 9: 683, 1922.

Soret. Radium therapy of roentgen ray burns. *Paris méd.*, 1: 534, 1928.

Stenstroem, K. W. A new device for retubing radium emanation. *Am. J. Roentgenol.*, 10: 311, 1923.

Stevens, J. T. Ray treatment of cancer. *N. York M. J.*, 116: 386, 1922.

Stevenson, W. C. A method of recording radium doses. *Arch. Radiol. & Electroth.*, 20: 270, 1916.

Stevenson, W. C. Notes on three cases of peritonitis treated by radium. *Dublin J. M. Sc.*, 4: 632, 1922.

Stone, W. S. The present field for use of x-rays and radium in the treatment of malignant neoplasms. *Am. J. Roentgenol.*, 9: 502, 1922.

Strasburger, J. Treatment with radium emanation. *Strahlentherapie*, 13: 528, 1921–22.

Strasburger, J. Improved utilization of radium emanation by combining it with fat. *Deutsche med. Wchnschr.*, 49: 1459, 1923.

Taussig, L. R. A report of the work of the radium department of the University of California Hospital between April, 1920 and April, 1921. *California State J. M.*, 20: 50, 1922.

Thompson, E. J. Ménière's syndrome following the use of radium. *J. A. M. A.*, 82: 388, 1924.

Tizzoni, G., Cetanni, E., and de Angelis, G. Modification produced by radium on emulsion of adenocarcinoma of mouse and its transformation into curative vaccine. *J. Trop. Med.*, 28: 438, 1925.

Tomanek, F. The results of radium therapy in pernicious anemia. *Cas. lek. cesk.*, 63: 549, 1924.

Tomanek, F. Present and future of radium and x-ray treatment. *Brit. J. Radiol.*, 31: 255, 1926.

Tousey, S. Treatment with radium. *Internat. Clin.*, s. 34, 2: 71, 1924.

Tousey, S. Progress in x-ray and radium therapy. *Physical Therapy*, 44: 423, 1926.

Turner, D. The use of radium in the treatment of disease. *Brit. M. J.*, 1: 464, 1923.

Viol, C. H. Some units and terminology used in radium and emanation therapy. *Radium*, 1: 9, 1913.

Viol, C. H. Protection of technical assistants and of those handling large quantities of radium or radon. *Am. J. Roentgenol.*, 15: 345, 1926.

Wachtel, H. New devices for the implantation and removal of radium needles. *Am. J. Roentgenol.*, 15: 76, 1926.

Wakeley, C. P. G. Radium carcinoma of thumb. *Brit. J. Surg.*, 14: 677, 1927.

Weed, W. A. The present status of the local application of radium and x-rays. *N. York M. J.*, 107: 495, 1918.

Werner, R., and Borchard, E. The curability of malignant new growths. *Deutsche med. Wchnschr.*, 50: 3, 1924.

Wood, F. C. Effect on tumors of radiation of different wave-lengths. *Am. J. Roentgenol.*, 12: 474, 1924.

Yamasaki, I. Radium hemolysis. *Strahlentherapie*, 29: 363, 1928.

Young, W. J. Treatment of malignant conditions with radium. *Kentucky M. J.*, 19: 778, 1921.

Young, W. J. X-ray and radium treatment of cancer. *Kentucky M. J.*, 19: 812, 1921.

Zeisler, J. An unknown case of multiple benign sarcoid of the skin. *J. A. M. A.* 65: 764, 1915.

Zweifel, E. Radiotherapy in carcinoma. *Arch. f. Gynäk.*, 117: 269, 1923.

Books

Colwell, H. A. and Wakeley, C. P. An Introduction to the Study of X-rays and Radium. Oxford Univ. Press, 1926.

Clark, J. G., and Norris, C. C. Radium in Gynecology. Phila., Lippincott, 1927.

Dominici, H. M. D., and Warden, A. A. The Technique and Results of Radium Therapy in Malignant Diseases. Lond., Churchill, 1912.

Finzi, N. S. Radium Therapeutics, Oxford Univ. Press, 1913.

Janeway. Radium Therapy in Cancer at the Memorial Hospital. N. Y., Hoeber, 1917.

Knox. Radiography and Radiotherapeutics. N. Y., Macmillan, 1918.

Knox, R. Radiography and Radio therapeutics. Ed. 3, Lond., 1919, Part 2, p. 520.

Knox, R. Radium in diseases of the eye. Part II. Radiography and radiotherapeutics. Ed. 3, 1919, p. 516. London, A. & C. Black; New York, MacMillan Co.

Lazarus, P. Handbuch der Radium-Biologie und Therapie. Preface by Prof. Dr. Friedrich Kraus. Wiesb., 1913, J. F. Bergmann. 538 p. 2 pl. 4°.

Memorial Hospital, Radium Report of, N. Y., Hoeber, 1923.

Newcomet. Radium and Radiotherapy. Lea & Febiger, 1914.

Rutherford. Radio-Active Substances and Their Radiations. Cambridge Univ. Press, 1913.

Simpson, F. E. Radium Therapy. St. Louis, Mo. C. V. Mosby, 1922.

Soddy. The Chemistry of the Radio Elements. N. Y., Longmans Green, 1911–1914.

Soddy. The Interpretation of Radium and the Structure of the Atom. N. Y., Putnam's Sons, 1920.

Wickhan and Degrais. Radium Therapy. N. Y., Funk & Wagnalls, 1912.

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